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IN THIS ISSUE

Incidence of Cancer in Atlanta, Ga., and Adjacent Counties

Allergic Irritability in Rheumatic and Nephritic Patients

Treatment of Tumors in Mice by Phenanthrene Derivatives

Census Bureau Reports New Low Mortality Rates in 1938



UNITED STATES PUBLIC HEALTH SERVICE

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It contains (1) current information regarding the prevalence and geographic distribution of communicable diseases in the United States, insofar as data are obtainable, and of cholera, plague, smallpox, typhus fever, yellow fever, and other important communicable diseases throughout the world; (2) articles relating to the cause, prevention, and control of disease; (3) other pertinent information regarding sanitation and the conservation of the public health.

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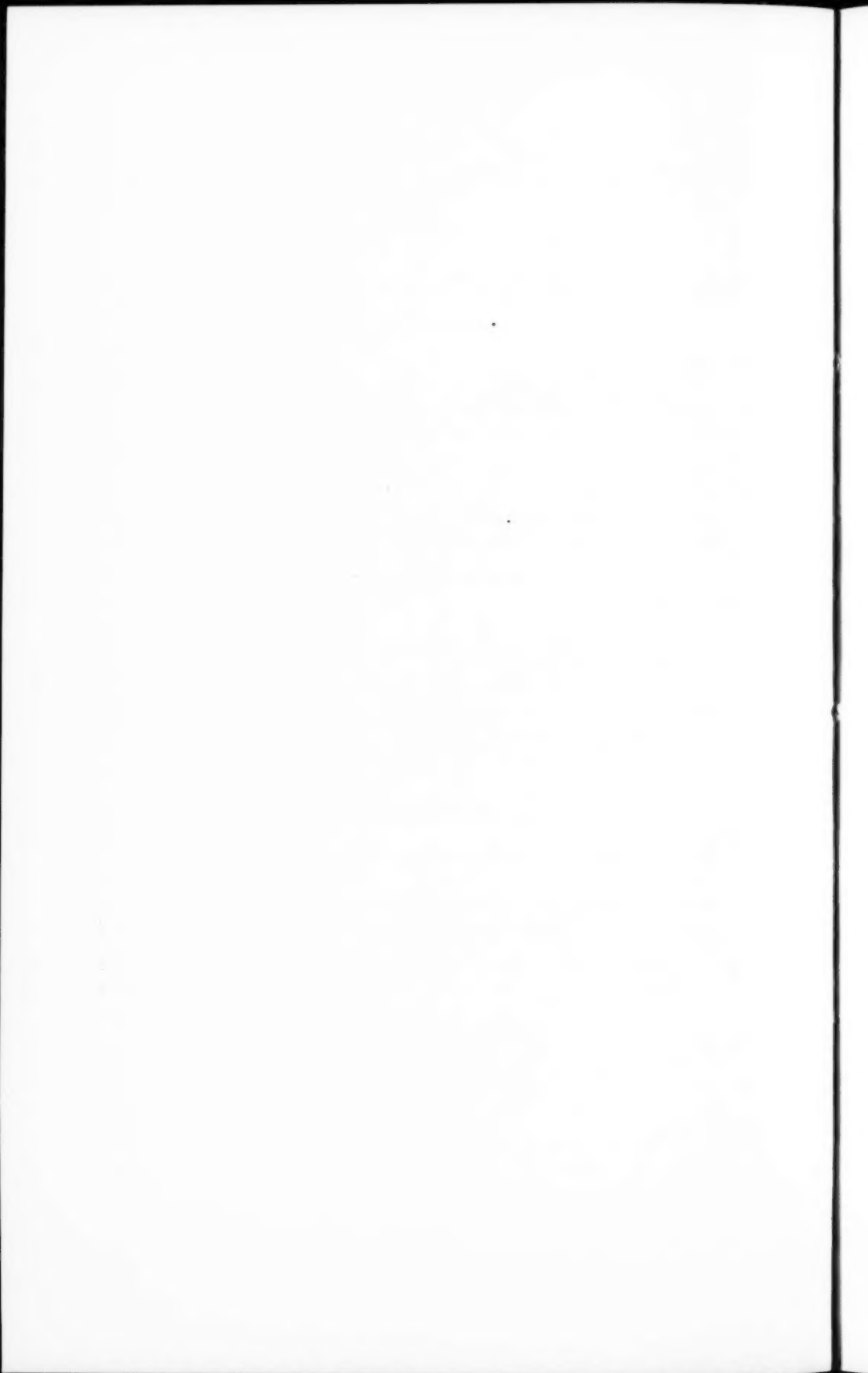
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Public Health Reports

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PREVALENCE OF POLIOMYELITIS

For the week ended July 8, 1939, the poliomyelitis situation, so far as the country as a whole is concerned, remained about the same as during the preceding week. A total of 84 cases was reported for the current week, as compared with 80 for the week ended July 1 and with a 5-year median of 156.

Only 8 States reported 4 or more cases for the week ended July 8, and only 3 States reported more than 6 cases. As compared with the preceding week, South Carolina dropped from 29 to 20 cases, North Carolina increased from 3 to 6, Georgia from 4 to 10, Florida from 0 to 4, and California from 16 to 18.

The relative significance of these figures is best shown by case rates. The figures for the week ended July 8 give South Carolina an annual rate of 55 per 100,000 population, North Carolina 9, Georgia 17, Florida 12, and California 15. Wyoming, with only 1 case, had a rate of 22, and Arizona, with only 1 case, a rate of 12. With the exception of South Carolina, this index of prevalence of poliomyelitis for the week is not as high in some of the States reporting the largest numbers of cases as that of less populous States reporting a smaller number.

THE INCIDENCE OF CANCER¹ IN ATLANTA, GA., AND SURROUNDING COUNTIES²

By JOSEPH W. MOUNTIN, *Senior Surgeon*, HAROLD F. DORN, *Statistician*, and BERT R. BOONE, *Passed Assistant Surgeon, United States Public Health Service*

For more than half a century, the increase in the number of deaths attributed to cancer in the mortality reports of most countries has attracted the attention of physicians, vital statisticians, public health officials, and biologists as well as that of the general public. However, no general agreement has been reached as to whether the recorded increase is real or spurious in the sense that it results from improved

¹ For the purpose of this study, reports were requested concerning every patient seen, observed, or treated for any malignant growth.

² From the Division of Public Health Methods in cooperation with the National Cancer Institute, National Institute of Health.

methods of diagnosis and increased accuracy in the certification of the cause of death, combined perhaps with greater care in searching for cancer. That cancer is an important medical problem is revealed by the fact that about 83 out of every 1,000 males and 115 out of every 1,000 females will die from cancer if the present reported mortality rates continue unaltered.

In spite of the interest aroused by the recorded increase in cancer mortality, very little information of general validity is available concerning the number of living persons who are afflicted with the disease. Statements are frequently made that certain types of cancer occur more frequently in one population group than in another, but these are usually based on the records of a particular institution or institutions and, consequently, may not be representative of conditions in the general population.

Although the records of individual clinics or hospitals may yield valuable data bearing upon many questions related to the occurrence and treatment of cancer, the answer to a great variety of such questions can be best obtained by an investigation of the prevalence of cancer in the general population. How many people are known to have cancer? What parts of the body are most frequently attacked? Does climate affect the occurrence of cancer? Is cancer more common among Negroes than among white persons? Which groups are attacked most frequently? Do persons living in the open country have more or less cancer than persons living in cities? The answers to these and many similar questions depend upon a careful epidemiological investigation of cancer in representative population groups.

Moreover, these and many similar questions cannot be completely answered by the use of mortality statistics alone. It is well known that some cancers are more likely to be fatal than others. For example, cancer of the stomach terminates in death more frequently than cancer of the skin of the face. Consequently, conclusions drawn from mortality records will differ from those drawn from morbidity reports not only as to the amount of cancer but also as to the tissues or organs involved. Furthermore, as methods of therapy become more effective, the types of cancer most easily arrested will appear less and less frequently in mortality records.

Because of these considerations, a series of studies has been initiated to determine the morbidity from cancer, its variation from one part of the country to another, between the two sexes, between whites and Negroes, and at different ages. If the results of such studies are to be the basis of projection, the data should pertain to the total population of a given community and should be obtained preferably from physicians and hospitals. Previous studies have shown that information concerning the morbidity from cancer collected by means of a house-to-house canvass results in only partial reporting,

since many people do not know that they have cancer and others will not admit the fact even if they know it to be true.

Various estimates have been made of the number of persons with cancer. The most widely quoted figure is three cases per recorded death, although some believe that there may be only two cases per recorded death. These estimates, however, are based on very fragmentary data and cannot be accepted as established. Moreover, it is quite possible that the morbidity from cancer varies from one part of the country to another so that no one figure is universally applicable.

It should be remembered that, regardless of how the incidence of cancer is expressed, either as the number of cases per death or as the number of cases per 1,000 population, the estimated figure will partially depend upon the effectiveness of methods of therapy and upon the stage at which the disease is recognized. It is impracticable, if not impossible, to obtain information for other than diagnosed cases of cancer. Obviously, no information concerning persons with undiagnosed cancer or with precancerous conditions is available. Consequently, the incidence of cancer referred to in this paper is the number of known or diagnosed cancer cases.

In a community where cancer is not recognized until the disease is far advanced, the number of cases will be only slightly greater than the number of deaths. For example, if each case lives just 1 year after diagnosis of cancer is made, the case rate of illness in any given year will be equal to the mortality rate of the following year. On the other hand, if each case lives 5 years, on the average, after diagnosis, the case rate of illness at any time will be five times the mortality rate 5 years later. While the effect of delayed diagnosis cannot be entirely eliminated, an attempt has been made to minimize its influence by undertaking the study only in areas with superior medical, hospital, and clinical facilities that are reasonably accessible to all groups of the population.

For the purpose of determining the incidence of cancer throughout the United States, several communities were selected in which studies of the type described are being conducted. Only the results of the first study are discussed in this paper. In addition to the city of Atlanta, the territory included Cherokee, Clayton, Cobb, De Kalb, Douglas, Fayette, Forsythe, Fulton, and Gwinnett Counties, all of which center around Atlanta. The total population of the area in 1930 was 511,000, of which 308,000 lived in urban localities (places with 2,500 or more population) and 203,000 lived in rural areas. About one-fourth of the population was Negro.

Since this is the first in a series of similar inquiries, the general plan and technique will be described in some detail. The study was conducted with the endorsement and cooperation of the State

Schedule used in survey of incidence of cancer

[This information is confidential and will be used for statistical purposes only]

Name of patient (please print)		City or county Actual residence not post office address	Sex M or F	Color W or C	Age Jan. 1, 1939	Alive Jan. 1, 1939 Yes or no	First seen with cancer		Last treated for cancer		Last seen (Includes cases still observed but no longer treated for cancer)		Micro- scopic diag- nosis (yes or no)	Type of cancer	Primary site if observed of skin, ear, or as "skin" of _____	Other sites in- volved (Enter each site involved even if it has been treated by sur- gery, X- ray, or radium)
Surname	First name, initial, and Mr., Mrs., or Miss						Mo.	Year	Mo.	Year	Mo.	Year				
Sample entry: Doe		Atlanta	F	W	57	Yes	April	1936	Dec.	1937	Nov.	1938	Yes	Epithelioma	Lip	None.
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1																
2																
3																
4																
5																
6																
7																
8																
9																
10																

If you have no case, write "no case" and return.
 Report every patient, including those in hospitals, whom you have seen, observed, or treated for any malignant or probably malignant growth at any time from January 1, 1938, to December 31, 1938, inclusive.
 Report every case even though the patient is now dead.
 Report every case even though referred for treatment.
 Report every case which you have treated prior to January 1938 but which still reports to you for observation.
 If you have not seen, treated, or observed any case during this 12-month period write "no case" in the space below and return this form to the United States Public Health Service in the accompanying addressed envelope which requires no postage.

and local health departments and the local medical and hospital societies. Reports were solicited only from physicians, hospitals, and clinics, but an effort was made to obtain a response from every such source. The schedule form used made provision for recording name, address, sex, color, and age of the patient, whether alive or dead, date first seen, dates last seen and last treated for cancer, method of diagnosis, and site or sites affected; forms were mailed to each physician, hospital, and clinic in the area. The field staff assisted in compiling the data from office records when requested to do so by the respondent. A personal visit was made to every physician, hospital, and clinic that failed to return the form promptly. Less than 3 percent of the potential respondents failed to cooperate.

In studies of this nature it is essential to eliminate two important types of error. One arises from the fact that many cancer cases are seen or treated by more than one physician; the other results from the fact that a certain proportion of the cases under treatment at any time will be nonresidents. Failure to correct for the effect of either of these sources of error would fictitiously increase the case rate of illness from cancer in the population under study. By securing the name and the county or city of residence for each patient it was possible to distinguish nonresident cases and those reported more than once.

The importance of eliminating these two sources of error is revealed by the fact that 32 percent of the reported cases were not residents of the area and that 17 percent of the cases were reported by more than one respondent. The duplicate cases, 540 in all, were reported 1,249 times. If the duplicates had not been detected the number of cases would have been increased 22 percent.

The number of reported cases of cancer among residents of the area was 2,164. In addition, information was obtained for 1,036 nonresident cases, making a total of 3,200 cases.³ During the year 1937, 425 deaths among residents of the study area attributed to cancer were reported to the State health department. All except 99 of these deaths were reported as cases by a physician, hospital, or clinic in connection with the incidence study.

The fact that 23 percent of the recorded deaths of residents of the area were not reported as cases should not be interpreted as meaning that a corresponding proportion of living cases were unreported. Investigation revealed that a large proportion of the certificates for these deaths were attested to by the health officer or coroner without having attended the case; in other instances the deaths were certified by a physician who had subsequently died or moved away. When-

³ With the exception of the data in table 3, which are based on resident cases and deaths, the following discussion refers to all cases reported, both resident and nonresident. The data were tabulated by residence, but since the two sets of cases were apparently very similar they were combined except when specifically stated otherwise.

ever the physician who signed the death certificate could be located, he was requested to supply information concerning the case, but not infrequently he would report that the case had been attended only at death and consequently he had only limited knowledge of the condition. It is believed that a small number of the cases of cancer also were not reported by some physicians who had to depend upon their memory instead of written records. As a rule these physicians were in general practice and saw only a limited number of cancer patients or even none at all. The actual number of cases of cancer among residents of the territory may, therefore, be somewhat larger than that actually reported.

About one-half of the physicians stated that they either did not treat cancer or that they had treated none during the study year, 1937. Less than 10 percent of the physicians reported more than five cases. Slightly more than one-half of the cases were obtained only from hospitals or clinics, 36 percent were reported only by physicians, and the remaining 12 percent were reported by combinations of these sources.

Since the value of a study of this nature depends not only on the completeness with which the cases are reported but also on the accuracy with which the diagnosis is made, each respondent was requested to specify whether or not the diagnosis of cancer was confirmed by a microscopic examination of tissue. The tissue for such examination may have been obtained through biopsy, operation, or post mortem. The reports showed that microscopic examination was made for slightly more than one-half of the reported cases (table 1). However, 61 percent of the cases receiving treatment from a hospital or clinic had the diagnosis confirmed by microscopic examination of tissue, as compared with only 37 percent of the cases not reported by a hospital or clinic.

TABLE 1.—*Number and percentage of cases of cancer with a microscopically confirmed diagnosis, by sex, color, and whether or not reported by a hospital, Atlanta, Ga., and surrounding territory, 1937*

Sex and color	Reported by hospital			Reported by physician only		
	Total number	Number with microscopic diagnosis	Percent	Total number	Number with microscopic diagnosis	Percent
White:						
Male.....	827	373	45.1	703	155	20.8
Female.....	950	669	70.4	598	257	43.0
Colored:						
Male.....	52	29	55.8	8	3	-----
Female.....	227	175	77.1	35	8	-----
Total.....	2,056	1,246	60.6	1,144	423	37.0

Irrespective of whether or not they were receiving treatment in a hospital, a larger proportion of women than of men were reported to have had a microscopically confirmed diagnosis. In part, at least,

this reflects the fact that the diagnosis of cancer of the uterus and breast, which comprises one-half of the reported cases among women, is confirmed by microscopic examination of tissue more frequently than the diagnosis of most other forms of cancer.

A microscopic method of diagnosis was reported for a larger proportion of the Negro than of the white cases. This is probably due to the fact that skin cancer, which makes up more than one-fourth of all types among white persons, is relatively rare among Negroes. The diagnosis of this type of cancer is frequently established without microscopic examination of tissue.

Whether or not the diagnosis of cancer is confirmed by a microscopic examination depends largely upon the accessibility of the tissue affected, especially for living cases. This is true irrespective of whether the patient is treated in a hospital, although, as a group, hospitalized cases of cancer have the diagnosis confirmed more frequently by microscopic examination of tissue than do cases not treated in a hospital. (When the records of dead cases are included, this statement must be modified, since many necropsies are performed on cases with "inaccessible" cancer.) In more than three-fourths of living and dead cases with cancer of the uterus, kidneys, bladder, and brain, the diagnosis was confirmed microscopically. On the other hand, only one-fifth of the diagnoses of skin cancer were confirmed microscopically (table 2), but, as stated previously, physicians commonly establish this diagnosis without tissue examination.

TABLE 2.—Percentage of cases of cancer by method of diagnosis, primary site, and whether or not reported by a hospital, Atlanta, Ga., and surrounding territory, 1937¹

Primary site	Percentage of cases with a microscopic diagnosis		
	Total	In hospital	Not in hospital
Buccal cavity, pharynx.....	47.7	54.8	34.8
Lip.....	28.5	36.4	14.7
Others.....	73.7	78.9	63.8
Digestive tract ²	50.0	52.7	43.7
Intestines, stomach, rectum, anus, duodenum.....	49.2	52.6	39.7
Others.....	52.3	52.9	51.4
Respiratory system.....	51.6	52.5	50.0
Genitourinary system.....	74.9	81.0	58.1
Uterus.....	79.9	86.0	61.1
Kidneys, bladder.....	77.5	82.0	67.9
Prostate.....	52.6	61.4	30.8
Others.....	67.6	70.4	59.4
Breast.....	73.2	81.9	53.4
Skin.....	21.3	20.6	9.9
Brain.....	81.1	71.4	82.1
All others.....	53.2	60.0	41.0
Total.....	52.2	60.6	37.0

¹The number of cases is given in the appendix, table 1.

²Includes mesentery and peritoneum.

There are several ways in which the incidence of cancer may be expressed. One expression would be analogous to a crude death rate, that is, the number of cases of cancer per 1,000 population. Since nearly 9 years has elapsed following the last general census of population, it is difficult to obtain accurate estimates of the population for small areas such as counties. Consequently it has been necessary to adopt another measure of incidence, namely, the ratio of the number of cases of cancer to the number of deaths from cancer. If a reasonably accurate estimate of the death rate is available, the case rate of illness can be estimated by multiplying the death rate by the ratio of cases to deaths, once the ratio of cases to deaths has been established.

The number of cases alive at any time during 1937 per recorded death from cancer was 5.3 (table 3). The death rate from cancer in this area was about 70 per 100,000 population at the date of the last census; hence the case rate of illness is at least 370 per 100,000 population. Since the death rate has undoubtedly increased since 1930, the case rate of illness in 1937 probably was at least 400 per 100,000 population, or 4 per 1,000 population.

TABLE 3.—Number of cases of cancer alive at any time during the year per recorded death from cancer during the year, by color and sex, Atlanta, Ga., and surrounding counties, 1937 (resident cases only)

Area	Total			White			Colored		
	Both sexes	Male	Female	Both sexes	Male	Female	Both sexes	Male	Female
Atlanta.....	5.3	4.9	5.6	5.8	5.7	5.8	4.0	2.3	4.9
Other urban localities.....	4.6	5.2	4.3	4.6	4.9	4.3
Total urban.....	5.3	4.9	5.4	5.6	5.6	5.6	4.0	2.5	4.9
Total rural.....	5.6	6.0	5.4	5.8	6.0	5.7	3.2	2.8
Total.....	5.3	5.1	5.4	5.7	5.7	5.6	4.0	2.5	4.7

The number of cases per death was markedly greater for whites (5.7) than for Negroes (4.0). These ratios indicate case rates of illness of at least 450 per 100,000 white population and 250 per 100,000 colored population (fig. 1).

The higher number of cases per death for the white population resulted in large part from the very low ratio for Negro males, 2.5; but the ratio for Negro females, 4.7, was also less than that for white females, 5.6. It seems likely that this difference between whites and Negroes arises in part from the fact that a larger proportion of Negroes than whites fail to obtain medical care until the disease is well developed; hence they do not live as long after diagnosis is established as do white persons who obtain treatment at an earlier stage of the disease. Moreover, the expectation of life of white persons is about 12 years greater than that for Negroes. Since cancer is especially

prevalent among persons in late adult life, a larger proportion of Negroes than of whites die from causes other than cancer before they reach the ages when cancer is most likely to develop. It is also possible that there either is less cancer or that it is more lethal among Negroes than among whites, but such an explanation should not be accepted until it can be shown that other factors do not account for the difference. The factor of site will be discussed later.

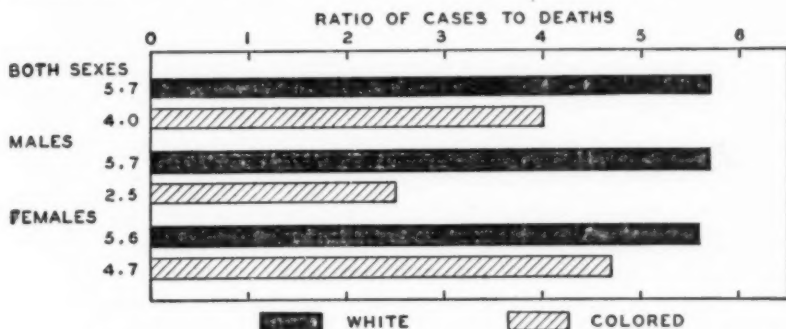


FIGURE 1.—Number of cases of cancer alive at any time during the year per recorded death from cancer during the year, by sex and color, Atlanta, Ga., and surrounding counties, 1937.

When interpreting the data in table 4, it should be remembered that the age distribution of the cases depends to a certain extent upon the age distribution of the population. Although cancer is often considered to be a disease of late adult life and old age, 449, or 14.0 percent, of the reported cases were less than 40 years of age. A slightly greater proportion of the women than of the men were less than 40 years of age, 16.2 percent as compared with 11.1 percent.

TABLE 4.—Number and percentage distribution by age and sex of cases of cancer, Atlanta, Ga., and surrounding counties, 1937

Age	Percentage			Number of cases		
	Total	Male	Female	Total	Male	Female
Under 9.....	0.7	0.8	0.7	25	12	13
10-19.....	1.2	1.8	.7	38	25	13
20-29.....	2.9	2.5	3.0	90	35	55
30-39.....	9.2	6.0	11.8	296	83	213
40-49.....	20.0	19.5	20.4	640	271	369
50-59.....	22.9	22.5	23.2	732	313	419
60-69.....	22.4	23.0	21.8	716	320	396
70-79.....	13.2	15.5	11.3	421	216	205
80 and over.....	4.7	5.5	4.3	152	75	77
Unknown.....	2.8	2.9	2.8	90	40	50
Total.....	100.0	100.0	100.0	3,200	1,390	1,810

About one-half of the persons with cancer were in what may be considered the main productive period of life, 30 to 60 years of age. The proportion for males in this age period, 48 percent, was slightly less than that for females, 55 percent.

The classification of the cases of cancer by type of lesion used in this paper follows that of the International List of Causes of Death. The advantages of being able to compare the results of this study with available mortality records were considered to outweigh the disadvantages of using the International List classification.

The skin was the most frequent site of cancer among males, accounting for 37 percent of the total reported cases (table 5). Among females, cancer of the skin, breast, and cervix each comprised about 20 percent of the total number of cases. With the exception of the fundus of the uterus no other site accounted for more than 3 percent of the total number of cancers among women. For the males, cancer of the lip and of the prostate made up 12 percent and 7 percent, respectively, of the total cancers, with the remaining cases widely scattered among the other sites. The greatest differences between the sexes are for cancer of the skin and lip, which are more frequent for males, and cancer of the breast, which is primarily a disease of the females. Lesions of the respiratory system and digestive tract are also more frequent among males.

TABLE 5.—Percentage distribution of cases of cancer by primary site, sex and color, Atlanta, Ga., and surrounding territory, 1937¹

Primary site	Total		White		Colored	
	Male	Female	Male	Female	Male	Female
Buccal cavity, pharynx.....	17.8	4.2	18.0	4.4	11.7	3.1
Lip.....	11.9	1.1	12.5	1.24
Tongue.....	1.5	.4	1.5	.5	1.7
Mouth.....	1.1	.6	1.1	.4	1.5
Jaw.....	1.2	.9	1.0	1.0	5.0	.4
Pharynx.....	.4	.1	.3	.1	1.7
Others.....	1.7	1.1	1.6	1.2	3.3	.8
Digestive tract.....	13.4	8.9	12.8	9.2	26.7	7.6
Esophagus.....	.6	.6	.6	.74
Stomach and duodenum.....	4.7	1.5	4.2	1.2	16.7	3.4
Intestines.....	3.5	3.0	3.4	3.2	5.0	2.3
Rectum and anus.....	2.3	1.9	2.4	2.17
Liver and biliary passages.....	.8	1.2	.7	1.3	1.7	.4
Pancreas.....	1.1	.5	1.1	.6	3.3
Mesentery and peritoneum.....	.4	.2	.4	.14
Respiratory system.....	3.7	.7	3.7	.7	3.3	.8
Larynx.....	1.2	.3	1.2	.24
Lungs and pleura.....	2.0	.4	2.0	.5	1.7	.4
Others.....	.55	1.6
Genitourinary system.....	12.6	36.0	11.3	32.7	40.0	55.3
Uterus (body).....	7.9	7.2	11.8
Cervix.....	21.8	18.9	38.9
Kidneys.....	.8	.9	.7	.9	3.3	.8
Bladder.....	2.7	1.4	2.5	1.6	5.0	.4
Prostate.....	7.0	6.2	25.0
Others.....	2.1	4.0	1.9	4.1	6.7	3.4
Breast.....	21.4	.1	21.1	22.9
Skin.....	36.9	20.4	38.5	23.1	1.7	4.2
All others.....	15.6	8.4	15.6	8.8	16.6	6.1
Total.....	100.0	100.0	100.0	100.0	100.0	100.0

¹ The number of cases is given in the appendix, table 3.

With the exception of cancer of the skin, no single lesion is predominantly frequent among males. Cases of cancer among females, on the other hand, are fairly well concentrated into three main groups—skin, breast, and uterus (fundus and cervix), which include more than 70 percent of all reported cancers (fig. 2).

There are a number of interesting differences in the relative frequency of various sites of cancer between whites and Negroes. It

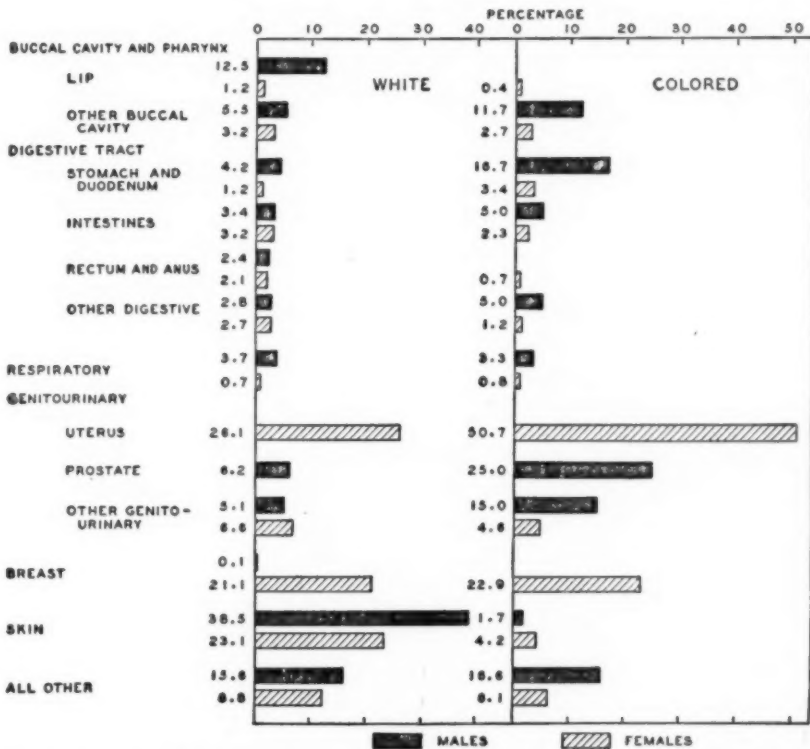


FIGURE 2.—Percentage distribution of cases of cancer by primary site, sex, and color, Atlanta, Ga., and surrounding counties, 1937.

should be remembered that the frequency of occurrence of various lesions depends to a certain extent upon the age distribution of the two groups since not all lesions develop at the same age. The number of cases of cancer among Negro males is too small to be more than merely indicative, but the distribution of sites affected is fairly reliable for Negro females. The most striking difference is the very low incidence of skin cancer among Negroes, 2 percent for males and 4 percent for females, compared with 38 percent and 23 percent, respectively, for white males and females. This is in agreement with the observation that skin diseases are generally less frequent in the Negro race. Cancer of the lip, which is a frequent site among white males, is also very rare among Negroes. The principal sites for Negro

females are the breast and genitourinary system. These include nearly 80 percent of all reported cases.

Since the various forms of therapy now in use are not uniformly effective against all types of lesions, and since some tumors are less malignant than others, the frequency of occurrence of different sites varies markedly between living and dead cases (table 6). Cancer of the skin, which accounts for 37 percent of the cases of cancer among males and 20 percent of the cases among females, comprises only 6

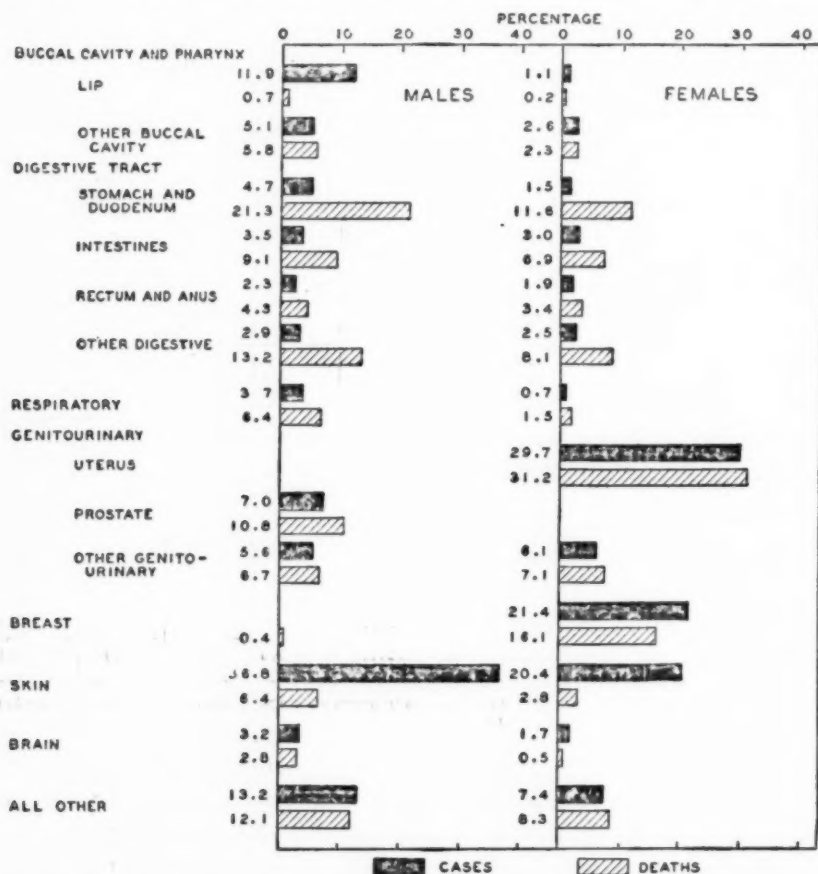


FIGURE 3.—Percentage distribution by primary site and sex of reported cases of cancer and recorded deaths from cancer, Atlanta, Ga., and surrounding counties, 1937. (Deaths are for the State of Georgia.)

percent of the male deaths from cancer and 3 percent of the female deaths. On the other hand, cancer of the digestive tract, which includes nearly 50 percent of all male deaths from cancer and 30 percent of all female deaths, is reported about one-fourth as frequently among living cases (fig. 3).

More than 40 percent of all deaths from cancer among males are attributed to the stomach, prostate, and intestines. Among females, the uterus, breast, and stomach comprise nearly 60 percent of all sites

reported on death certificates. The uterus and breast are the only two important sites reported with approximately the same relative frequency among both living and dead cases of cancer.

TABLE 6.—Percentage distribution by primary site and sex for reported cases and recorded deaths from cancer, Atlanta, Ga., and surrounding territory, 1937¹

Primary site	Male		Female	
	Cases	Deaths	Cases	Deaths
Buccal cavity, pharynx.....	17.0	6.5	3.7	2.5
Lip.....	11.9	.7	1.1	.2
Tongue.....	1.5	1.1	.4	.3
Mouth.....	1.1	1.2	.6	.6
Jaw.....	1.2	1.7	.9	.3
Pharynx.....	.4	1.1	.1	.8
Others.....	.9	.7	.6	.3
Digestive tract.....	13.4	47.9	8.9	30.0
Esophagus.....	.6	1.4	.6	1.0
Stomach and duodenum.....	4.7	21.3	1.5	11.6
Intestines.....	3.5	9.1	3.0	6.9
Rectum and anus.....	2.3	4.3	1.9	3.4
Liver, biliary passages.....	.8	7.6	1.2	5.7
Pancreas.....	1.1	3.7	.5	1.2
Mesentery, peritoneum.....	.4	.5	.2	.2
Respiratory system.....	3.7	6.4	.7	1.5
Larynx.....	1.2	.6	.3	.1
Lungs, pleura.....	2.0	4.4	.4	1.0
Others.....	.5	1.4		.4
Genitourinary system.....	12.6	17.5	35.8	38.3
Uterus.....			29.7	31.2
Kidneys.....	.8	1.4	.9	1.2
Bladder.....	2.7	3.3	1.4	2.2
Prostate.....	7.0	10.8		
Others.....	2.1	2.0	3.8	3.7
Breast.....		.4	21.4	16.1
Skin.....	36.9	6.4	20.4	2.8
Brain.....	3.2	2.8	1.7	.5
Bones (except jaw).....	1.4	1.2	1.0	.6
All others.....	11.8	10.9	6.4	7.7
Total.....	100.0	100.0	100.0	100.0

¹ In order to have a sufficiently large number of deaths to provide a stable distribution by site, the number of deaths for the entire State of Georgia was used.

Table 7 presents the proportion of cases of cancer of certain primary sites with a recognized and reported metastasis. Whether or not the reported lesion had metastasized from the original primary site depends upon many factors, among them the stage of the disease at which treatment was begun, and the thoroughness of the examination. Slightly more than one-fourth of the persons with cancer were reported to have a metastatic lesion. This proportion varies widely from one site to another. The primary sites with the smallest percentage of metastases are the brain, skin, bladder, and lip, less than one-fifth of each having one or more additional sites reported, while the sites with most frequent metastasis are the breast, stomach, and intestines, nearly one-half of which had a secondary involvement. A high percentage of metastases was also reported for several other sites but the number of cases involved is too small to permit definite conclusions.

TABLE 7.—*Number and percentage of cancer cases with reported metastasis, by primary site, Atlanta, Ga., and surrounding territory, 1937*

Primary site	Total number	Number with metastasis	Percent with metastasis
Buccal cavity.....	323	66	20.4
Lip.....	186	28	15.1
Tongue.....	29	10	34.5
Mouth.....	25	10	40.0
Jaw.....	33	6	18.2
Pharynx.....	6	2	33.3
Others.....	44	10	22.7
Digestive tract.....	348	128	36.8
Esophagus.....	20	5	25.0
Stomach, duodenum.....	93	38	40.9
Intestines.....	93	39	41.9
Rectum, anus.....	66	15	22.7
Liver, biliary passages.....	33	14	42.4
Pancreas.....	25	13	52.0
Mesentery, peritoneum.....	8	4	50.0
Respiratory system.....	64	19	29.7
Larynx.....	21	2	9.5
Lungs, pleura.....	36	13	36.1
Others.....	7	4	57.1
Genitourinary system.....	826	228	27.6
Uterus (body).....	141	41	28.7
Cervix.....	395	87	22.0
Kidney.....	27	10	37.0
Bladder.....	62	11	17.7
Prostate.....	97	29	29.9
Others.....	102	50	49.0
Breast.....	388	176	45.4
Skin.....	882	155	17.6
Brain.....	74	4	5.4
Bones.....	28	10	26.3
All others.....	257	56	21.8
Total.....	3,200	842	26.3

The data in table 8 and figure 4 show that lesions of certain organs or tissues develop at a younger age than those of other organs. Although cancer is primarily a disease of late adult life and old age, some forms occur predominantly in young persons. The outstanding example of the latter is cancer of the brain. More than one-half of the persons with cancer of the brain were less than 35 years old. The number of reported cases was fairly small so that the percentage distribution by age is somewhat irregular, but the general tendency is unmistakable. Other sites reported frequently at the younger ages were the kidneys, bladder, and respiratory system.

Cancer of the prostate, on the other hand, occurs mainly among the aged, 78 percent of the reported cases being 65 or more years of age. About 40 percent of the persons with cancer of the skin were also 65 or more years of age.

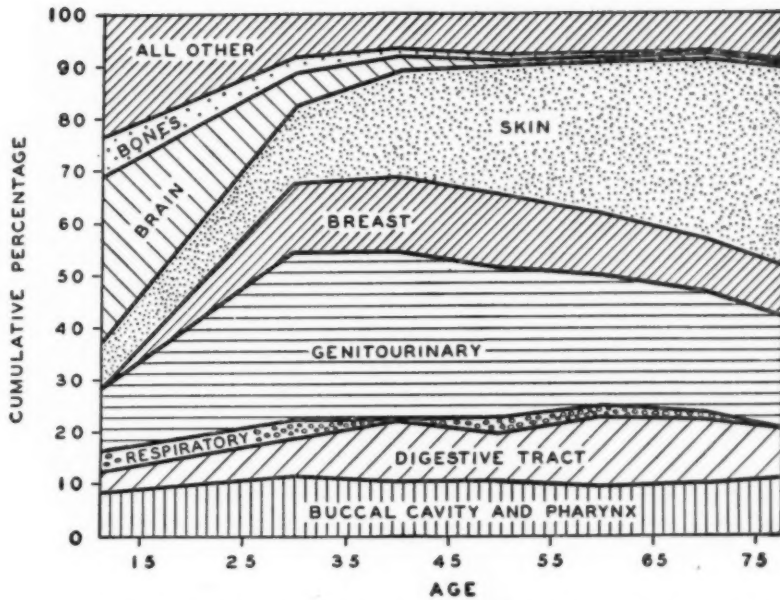


FIGURE 4.—Percentage distribution of cases of cancer by age and primary site, Atlanta, Ga., and surrounding counties, 1937.

TABLE 8.—Percentage distribution of cases of cancer by age and primary site, Atlanta, Ga., and surrounding territory, 1937¹

Primary site	Age in years							
	Under 25	25-34	35-44	45-54	55-64	65-74	75 and over	Unknown
Buccal cavity, pharynx.....	2.5	5.9	15.8	23.8	22.3	18.0	10.2	1.5
Lip.....	2.2	6.5	16.7	24.7	18.8	22.0	7.0	2.1
Others.....	2.9	5.1	14.6	22.6	27.0	12.4	14.6	.8
Digestive tract ²	1.2	3.2	16.4	17.5	28.4	21.3	8.6	3.4
Stomach, intestines, rectum, anus.....	1.5	3.0	17.1	18.6	26.6	26.2	9.1	3.8
Others.....		3.5	14.1	14.1	34.1	24.7	7.1	2.4
Respiratory system.....	4.7	7.8	3.1	32.8	26.6	14.1		10.9
Genitourinary system.....	1.4	6.2	19.1	23.5	23.1	16.5	8.0	2.2
Uterus.....	.4	7.4	24.5	27.5	21.8	12.6	4.1	1.7
Prostate.....			1.0	6.2	21.7	43.3	24.7	3.1
Kidneys, bladder.....	6.7	3.4	6.7	13.5	36.0	18.0	11.2	4.5
Others.....	3.9	7.8	18.6	27.5	20.6	9.8	9.8	2.0
Breast.....		5.7	19.1	25.5	23.4	14.7	7.2	4.4
Skin.....	.9	2.6	11.2	19.4	24.8	23.7	15.3	2.1
Brain.....	40.5	13.5	18.9	10.8	14.9	1.4		
All others.....	9.8	6.1	13.6	19.3	20.3	15.9	10.5	4.5
Total.....	2.9	5.0	15.5	21.5	23.8	18.4	10.1	2.8

¹ The number of cases is given in the appendix, table 4.

² Includes mesentery and peritoncum.

SUMMARY

Three thousand two hundred cases of cancer were reported under observation or treatment in Atlanta, Ga., and surrounding territory during 1937. Of these, 2,164 were residents and 1,036 were nonresidents of the area.

The number of cases per recorded death attributed to cancer was 5.3 for the total population, 5.7 for the white population, and 4.0 for the colored population. These ratios correspond to case rates of illness of approximately 400, 450, and 250 per 100,000 population, respectively. The lower rate among Negroes may result from failure to seek medical care and a shorter length of life. It is also possible that cancer (total and for certain sites) really is less common in the colored population.

About one-half of the persons with cancer were in the main productive period of life, namely, 30 to 60 years of age. However, 14 percent of the reported cases were less than 40 years of age.

The most frequent site of cancer among males was the skin, which comprised 37 percent of all reported cases. Among females, cancer of the skin, breast, and cervix each made up about 20 percent of the total number of cases. Cancers of the skin and lip, respiratory system, and digestive tract were more frequent among males, while cancer of the breast and genitourinary system were more common among females.

Cancer of the skin, which accounted for 38 percent of all lesions among white males and 23 percent among white females, included only 2 percent of all lesions among Negro males and 4 percent among Negro females. Cancer of the lip is also rare among Negroes. Lesions of the breast and genitourinary system included nearly 80 percent of all reported sites for Negro females.

There are large differences in the frequency with which different kinds of cancer are reported for living and dead cases. More than 40 percent of all male deaths attributed to cancer are from lesions of the stomach, prostate, and intestines, which comprise only 15 percent of the reported lesions among living cases.

Among females, lesions of the breast, uterus, and stomach are reported for nearly 60 percent of the deaths assigned to cancer. Of these, lesions of the breast and uterus are the only ones which occur with approximately the same relative frequency among both living and dead cases of cancer.

Cancer of the digestive tract, to which is attributed nearly 50 percent of all male deaths from cancer and 30 percent of all female deaths, makes up only about one-fourth as large a proportion of the lesions of living cases.

Although cancer is primarily a disease of late adult life, certain types of lesions occur rather frequently in young persons. More than one-

half of the persons with cancer of the brain were less than 35 years old. Cancer of the kidneys, bladder, and respiratory system was also reported frequently among young persons.

APPENDIX

TABLE 1.—Number of cases of cancer by method of diagnosis, primary site, and whether or not reported by a hospital, Atlanta, Ga., and surrounding territory, 1937

Primary site	Number of cases reported			Number of cases with microscopical diagnosis		
	Total	In hospital	Not in hospital	Total	In hospital	Not in hospital
Buccal cavity, pharynx.....	323	208	115	154	114	40
Lip.....	186	118	68	53	43	10
Others.....	137	90	47	101	71	30
Digestive tract ¹	348	245	103	174	129	45
Intestines, stomach, rectum, anus, duodenum.....	262	194	68	129	102	27
Others.....	86	51	35	45	27	18
Respiratory system.....	64	40	24	33	21	12
Genitourinary system.....	826	609	217	619	493	126
Uterus.....	538	407	131	430	350	80
Kidneys, bladder.....	89	61	28	69	50	19
Prostate.....	97	70	26	51	43	8
Others.....	102	71	32	69	50	19
Breast.....	388	270	118	284	221	63
Skin.....	882	487	395	188	149	39
Brain.....	74	7	67	60	5	55
All others.....	295	190	105	157	114	43
Total.....	3,200	2,056	1,144	1,669	1,246	423

¹ Includes mesentery and peritoneum.

TABLE 2.—Number of reported cases of cancer and number of recorded deaths from cancer by color and sex, Atlanta, Ga., and surrounding counties, 1937¹

Area	Reported cases				Deaths not reported as a case				Total recorded deaths			
	White		Colored		White		Colored		White		Colored	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Atlanta.....	469	815	52	239	19	25	13	15	85	144	28	52
Other urban places.....	71	95	4	3	3	4	1	1	15	23	1	1
Total urban.....	540	910	56	242	22	29	13	16	100	167	28	53
Total rural.....	173	231	2	10	6	9	4	4	30	42	5	5
Total.....	713	1,141	58	252	28	38	13	20	130	209	28	58

¹ Includes only resident cases and deaths.

TABLE 3.—*Number of cases of cancer by primary site, sex, and color, Atlanta, Ga., and surrounding territory, 1937*

Primary site	Total		White		Colored	
	Male	Female	Male	Female	Male	Female
Buccal cavity, pharynx.....	247	76	240	68	7	8
Lip.....	166	20	166	19	-----	1
Tongue.....	21	8	20	8	1	-----
Mouth.....	15	10	15	6	-----	4
Jaw.....	16	17	13	16	3	1
Pharynx.....	5	1	4	1	1	-----
Others.....	24	20	22	18	2	2
Digestive tract.....	186	162	170	142	16	20
Esophagus.....	8	12	8	11	-----	1
Stomach and duodenum.....	66	27	56	18	10	9
Intestines.....	48	55	45	49	3	6
Rectum and anus.....	32	34	32	32	-----	2
Liver and biliary passages.....	11	22	10	21	1	1
Pancreas.....	16	9	14	9	2	-----
Mesentery and peritoneum.....	5	3	5	2	-----	1
Respiratory system.....	51	13	49	11	2	2
Larynx.....	16	5	16	4	-----	1
Lungs and pleura.....	28	8	27	7	1	1
Others.....	7	-----	6	-----	1	-----
Genitourinary system.....	175	651	151	506	24	145
Uterus (body).....	-----	143	-----	112	-----	31
Cervix.....	-----	395	-----	293	-----	102
Kidneys.....	11	16	9	14	2	2
Bladder.....	37	25	34	24	3	1
Prostate.....	97	-----	82	-----	15	-----
Others.....	30	72	26	63	4	9
Breast.....	1	387	1	327	-----	60
Skin.....	513	369	512	358	1	11
All others.....	217	152	207	136	10	16
Total.....	1,390	1,810	1,330	1,548	60	262

TABLE 4.—Number of cases of cancer by age and primary site, Atlanta, Ga., and surrounding territory, 1937

Primary site	Age in years										Total
	Under 14	15-24	25-34	35-44	45-54	55-64	65-74	75-84	85 and over	Un-known	
Buccal cavity, pharynx.....	2	6	19	51	73	72	58	30	3	5	323
Lip.....	1	3	12	31	46	35	41	12	1	4	186
Tongue.....			1	6	8	8	1	4	1		29
Mouth.....				2	7	7	6	2			24
Jaw.....	1	2	1	3	8	6	5	5	1	1	33
Pharynx.....			1		1	5					7
Others.....		1	4	9	7	11	5	7			44
Digestive tract, mesentery, peritoneum.....	1	3	11	57	61	99	74	26	4	12	348
Esophagus.....				2	3	8	6			1	20
Stomach, duodenum.....		1	2	19	17	25	20	8		4	96
Intestines.....		2	2	18	18	28	21	7	2	4	102
Rectum, anus.....	1		4	8	14	17	12	6	1	2	65
Liver and biliary passages.....				4	3	13	7	3	1	1	32
Pancreas.....			1	3	5	8	6	2			25
Mesentery, peritoneum.....			2	3	1		2				8
Respiratory system.....	2	1	5	2	21	17	9			7	64
Larynx.....			2		2	9	3			5	21
Lungs, pleura.....	2		3	1	18	5	6			2	37
Others.....		1		1	1	3					6
Genitourinary system.....	7	5	51	158	194	191	136	60	6	18	826
Uterus.....			8	31	44	35	15	5	2	3	143
Cervix.....	1	1	32	101	104	82	53	15		6	395
Kidneys.....	6			3	6	4	6	2			27
Bladder.....			3	3	6	28	10	7	1	4	62
Prostate.....			1	1	6	21	42	21	3	3	97
Others.....		4	8	19	28	21	10	10		2	102
Breast.....			22	74	99	91	57	27	1	17	389
Skin.....	3	5	23	99	171	219	209	109	29	18	882
Brain.....	16	14	10	14	8	11	1				74
Bones.....	2	5	5	8	6	7	4	1			88
All others.....	8	14	13	32	51	53	43	25	5	13	257
Total.....	41	53	159	495	688	760	591	278	45	90	3,200

ALLERGIC IRRITABILITY IN RHEUMATIC AND NEPHRITIC PATIENTS¹

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Allergic irritability, so-called by Lewis and Loomis (1), is easily demonstrable in animals suffering from chronic infections. For example, rabbits made allergic by suitable chronic focal infections, in contrast to controls, respond with both a primary and secondary reaction at the site of injection of nonspecific antigens, and also with an increased concentration of circulating antibodies (2). It was, therefore, thought possible that comparable, nonspecific alterations

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in tissue reactivity might result from certain infections in man. Focal infections, especially with hemolytic streptococci, have been considered of possible etiological significance in both rheumatic fever and acute hemorrhagic nephritis (3, 4, 5); and in patients with these diseases a marked cutaneous hypersensitivity to streptococcal products has been demonstrated (6, 7). It was the purpose of this investigation to study the nonspecific cutaneous reactivity to a simple foreign protein, such as rabbit serum, following focal infections in patients with these two diseases, and to compare this reactivity with the response of these patients to streptococcal nucleoprotein and tuberculin.

METHODS

On a given day the following materials were injected intracutaneously in different areas on the volar surface of the forearms, the respective test dose indicated being diluted to 0.1 cc. with normal salt solution:

1. 0.001 mg. of hemolytic streptococcus nucleoprotein (strain Q33), prepared by the method described by Lancefield (8).
2. 0.05 mg. of human tuberculin (O. T.).
3. 0.05 cc. of normal rabbit serum.

The reactions to nucleoprotein and tuberculin were recorded after 24 and 48 hours. For the purposes of the present study, lesions 20 by 20 by 1 mm. or larger, which were caused by the tuberculin, were considered positive. While reactions smaller than these were not infrequent, these responses seemed to give the best indications of the patients' reactivity with respect to the various agents. The areas injected with rabbit serum were inspected daily for 2 weeks or until a secondary reaction appeared. Neither immediate nor delayed 24-hour reactions were observed at the sites of serum injection. The responses of particular interest were the secondary reactions which occurred after 4 to 13 days, and which consisted of areas of edema and erythema as large as 70 by 70 by 2 mm. persisting for a few hours to several days. In all probability, these secondary reactions may be considered as local serum disease, and indicate the intensity of the patients' response to the introduction of the first dose of rabbit serum. It should be noted that they are different from the reactions, discussed by Mote and Jones (9), which resulted from repeated injections of this serum.

With serum obtained from bleedings made just prior to the injections and 2 weeks later precipitin tests were performed. Mixtures of 0.2 cc. of these sera were made with 0.4 cc. of rabbit serum dilutions ranging from 1:10 to 1:500,000. The mixtures were incubated 2 hours at 37° C. and refrigerated 8 hours; then the readings were made. Passive transfer tests were performed with the technique of

Prausnitz-Küstner (10); the site injected with 0.1 cc. of each serum tested was reinjected 24 hours later with 0.1 cc. of a 1:100 dilution of rabbit serum in normal saline. Each serum was tested on two volunteers, and controlled in each instance with serum from the preliminary bleeding.

RESULTS

There was no correlation apparent between the presence of carditis or arthritis, the degree of fever, or the age of the patient and the development of secondary reactions to rabbit serum. It also appeared that minimal therapeutic doses of antipyretic drugs, received by a few of the patients during the period of observation, were without demonstrable effect upon the outcome of the test.

In the instance of Bright's disease, it was impossible with the data at hand to dissociate the two factors of focal infection and the stage of the disease, for all patients in the acute hemorrhagic stage which were tested had also suffered recent focal infections.

A most important factor, however, associated with the type of response to intracutaneous injections of rabbit serum was recent focal infection. The findings are summarized in table 1. Secondary reactions were much more frequently observed in patients with rheumatic fever (46 percent) or Bright's disease (44 percent) than in controls (15 percent). It is apparent, moreover, that in both rheumatic and nephritic patients a recent focal infection was much more frequently accompanied by enhanced reactivity to rabbit serum than was the case with controls. Among the latter, secondary reactions were slightly more than twice as frequent in individuals with recent focal infections than in those not giving such a history. In rheumatic fever patients, on the other hand, secondary reactions were five times more frequent in those having recently suffered focal infections than in others. Because of the small number of patients with Bright's

TABLE 1.—Incidence of positive secondary reactions to rabbit serum

	Number of patients	Secondary reactions	
		Number	Percent
1. Rheumatic fever:			
With recent focal infection.....	35	31	88
Without recent focal infection.....	49	8	16
Total.....	84	39	46
2. Bright's disease:			
With recent focal infection.....	9	7	77
Without recent focal infection.....	7	0	0
Total.....	16	7	44
3. Other patients:			
With recent focal infection.....	12	3	25
Without recent focal infection.....	27	3	11
Total.....	39	6	15

disease the difference, though striking, may not be so significant. Nevertheless, there were no secondary reactions in seven individuals with no history of recent infection; while in seven of nine patients with recent infections secondary reactions developed.

REACTIONS TO HEMOLYTIC STREPTOCOCCUS NUCLEOPROTEIN AND TUBERCULIN

The groups tested with hemolytic streptococcus nucleoprotein or tuberculin are not strictly comparable. The average age of the control group was 34 years, the rheumatic 13, and the nephritic 20. It has been found that positive reactions to both these test substances are more frequent in older age groups (6). In patients with rheumatic fever there was a definitely greater incidence of positive reactions to hemolytic streptococcus nucleoprotein in individuals with recent focal infections than in the rheumatic group giving no history of comparable infections; such a difference was not evident in the incidence of positive tuberculin reactions (table 2). In the patients with Bright's disease a similar relationship was observed. The comparatively higher incidence of positive tuberculin reactions in the nephritic patients without recent focal infections is probably due to the fact that the average age of these patients (23 years) was somewhat greater than of those with recent infections (18 years). The relatively high incidence of positive reactions to nucleoprotein and tuberculin in the group of "other patients" (none with recent focal infection) also is probably due to the fact that this was definitely an older age group (average 34 years).

TABLE 2.—Incidence of positive reactions to hemolytic streptococcus nucleoprotein and tuberculin intracutaneously

	Number of patients	Positive reactions			
		Hemolytic streptococcus nucleoprotein		Tuberculin	
		Number	Percent	Number	Percent
1. Rheumatic fever:					
With recent focal infection.....	23	14	61	10	43
Without recent focal infection.....	37	13	35	16	43
Total.....	60	27	45	26	43
2. Bright's disease:					
With recent focal infection.....	8	3	37	1	12
Without recent focal infection.....	7	2	28	3	43
Total.....	15	5	33	4	27
3. Other patients:					
None with recent focal infection.....	23	11	48	15	65

One purpose in investigating the incidence of tuberculin and streptococcal nucleoprotein hypersensitivity in these patients was to test

the influence of these two states upon their reactivity to rabbit serum. No correlation could be established which appeared statistically significant except that among 66 patients who had not suffered recent focal infections no secondary reactions to rabbit serum were observed in the 24 who reacted negatively to both nucleoprotein and tuberculin.

CIRCULATING ANTIBODIES

Sera from 19 representative members of the several groups were tested for the presence of precipitins for rabbit serum, but there were no positive reactions. Agglutinin titers for rabbit red blood cells in the sera before and 2 weeks after the injection of rabbit serum were compared. The titers ranged from 1:40 to 1:160 with no indication of a significant change in any patient. Sera from the first and second bleedings were compared in 11 cases. The passive transfer of hypersensitivity by the Prausnitz-Küstner technique was attempted in 13 instances. A positive reaction, indicating the presence of antibodies in serum from the second bleeding, was obtained in only one case. This serum was from a rheumatic fever patient who had recently suffered a rather severe sore throat, and in whom a marked cutaneous secondary reaction to rabbit serum was observed. Because of the great difficulty in obtaining a large number of volunteers necessary for the testing of all the sera in this manner, these observations were not extended.

DISCUSSION

The phases of foreign protein sensitization in man and experimental animals have been reviewed by Rackemann (11). Two phases of hypersensitivity have been demonstrated: (1) One associated with a delayed response (the development of lesions only after 24 hours) and manifest in the absence of circulating antibodies; (2) a later stage in which an immediate reaction is obtained, the appearance of which is associated with the presence of antibodies in the blood serum. Since antibodies were demonstrated in the serum of only one of our patients among the number tested, it is probable that the secondary reactions observed appeared coincidentally with the development of the first stage of protein sensitization. Mote and Jones (9) have studied the phases of foreign protein sensitization in rheumatic fever patients, observing secondary reactions in 27 (52.8 percent) of 52 patients tested with 0.01 cc. of rabbit serum. Of these 27 this reaction was the first evidence of sensitivity in 22. These authors did not direct attention to a possible correlation between the allergic state of the individuals tested and the development of hypersensitivity. The secondary reactions they observed, moreover, appeared following repeated injections of foreign protein.

Our results indicate that, especially in patients with rheumatic fever or Bright's disease, focal infections are apt to be accompanied or followed by an increased degree of allergic irritability as demonstrated with rabbit serum.

This alteration in character of reactivity could not be correlated closely with the presence or absence of hypersensitivity to hemolytic streptococcus nucleoprotein or tuberculin. It was observed, however, in those individuals who had not experienced a recent focal infection, that no secondary reactions to rabbit serum occurred in the absence of hypersensitivity both to nucleoprotein and tuberculin.

These findings suggest that a focal infection is much more apt to increase the degree of allergic irritability in patients with rheumatic fever and Bright's disease than in controls.

SUMMARY

1. Increased allergic irritability, as demonstrated by the development of secondary reactions following the intracutaneous injection of small amounts of rabbit serum, occurred more frequently in patients with rheumatic fever or Bright's disease than in controls.

2. The incidence of this increased allergic irritability was greater in individuals who had recently suffered focal infections. This effect of infection was much more frequently observed in patients with rheumatic fever or Bright's disease than in controls.

3. Correlation between the presence of hypersensitivity to hemolytic streptococcus nucleoprotein or tuberculin and increased allergic irritability could be established only insofar as that among those individuals who had not recently experienced a focal infection no secondary reactions to rabbit serum were observed in the absence of hypersensitivity both to nucleoprotein and tuberculin.

4. These observations provide further evidence that alterations in tissue reactivity are associated with the rheumatic and nephritic states.

REFERENCES

- (1) Lewis, P. A., and Loomis, D.: Allergic irritability; influence of chronic infections and of trypan blue on formation of specific antibodies. *J. Exp. Med.*, **43**: 263 (1926).
- (2) Schultz, Mark P., and Swift, H. F.: Effect of antecedent infection and immunization with streptococci upon reactivity of rabbits to horse serum. *J. Exp. Med.*, **60**: 323 (1934).
- (3) Swift, H. F., Moen, J. K., and Hirst, G. K.: Action of sulfanilamide in rheumatic fever. *J. Am. Med. Assoc.*, **110**: 426 (1938).
- (4) Longcope, W. T., O'Brien, D. P., McGuire, J., Hansen, O. C., and Denny, E. R.: Relationship of acute infections to glomerular nephritis. *J. Clin. Invest.*, **5**: 7 (1927-28).
- (5) Winkelwerder, W. L., McLeod, N., and Baker, M.: Infection and hemorrhagic nephritis. *Arch. Int. Med.*, **56**: 297 (1935).
- (6) Kalsner, A. D., and Keith, J. D.: Cutaneous reactions to hemolytic streptococcus nucleoprotein in rheumatic and in nonrheumatic children. *N. Y. State J. Med.*, **35**: 69 (1935).

- (7) Longcope, W. T.: The pathogenesis of glomerular nephritis. *Bull. Johns Hopkins Hosp.*, **45**: 335 (1929).
- (8) Lancefield, R. C.: Immunological relationships of *Streptococcus viridans* and certain of its chemical fractions; serological reactions obtained with antinucleoprotein sera. *J. Exp. Med.*, **42**: 397 (1925). Antigenic complex of streptococcus hemolyticus; chemical and immunological properties of protein fractions. *Ibid.*, **47**: 469 (1928). Antigenic complex of streptococcus hemolyticus; chemical and immunological properties of specific substance. *Ibid.*, **47**: 481 (1928).
- (9) Mote, J. R., and Jones, T. D.: Development of foreign protein sensitization in human beings. *J. Immunol.*, **30**: 149 (1936).
- (10) Prausnitz, C., and Küstner, H.: Studien über die Überempfindlichkeit. *Centralb. f. Bakt. u. Parasit.*, **86**: 160 (1921).
- (11) Rackemann, F. M.: Review of phases of allergy. *J. Allergy*, **6**: 17 (1934).

EXPERIMENTAL TREATMENT OF TUMORS IN MICE ¹

I. BY PHENANTHRENE DERIVATIVES

By FLOYD C. TURNER, *Surgeon, United States Public Health Service, National Cancer Institute*

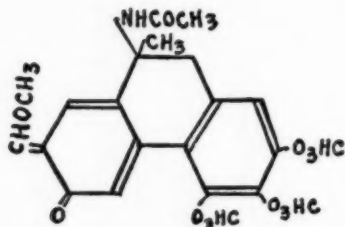
In seeking a logical approach to the treatment of tumors, it is found that salient facts are few and confusing. Many agents have caused experimental tumors in laboratory animals, for example, arsenic, viruses, coal tar, sex hormones, cancerigenic hydrocarbons, etc. In human beings, soot, radium paints, X-rays, betel-nut, sunlight, aniline dyes, and other agents have been suspected of being exciting etiological factors in tumor genesis (1). There appears to be no factor common to them all, yet conditions as different as X-radiation and polycyclic hydrocarbons affect tissues so that, by mutation or otherwise, a condition of irreversible unlimited proliferation is set up in certain cells.

One general difference between the physiology of normal and malignant tissues is that tumor tissue is ordinarily faster growing than normal tissue; there are proportionately more cells in the process of division in the cancerous tissues. An attempt was made to utilize that property therapeutically.

Colchicine affects mitosis both in animal and vegetable tissues (2). The mitoses of some cells are halted in the metaphase (3). There are also aberrant mitoses. The effects apparently cannot be satisfactorily prolonged. Malignant growths continue to grow grossly, in spite of poisonous doses. Regardless of this fact, however, colchicine does affect mitosis (4), which is evidence that there is some hope along this line of research. Some other chemical compound, of itself, or in combination with other therapeutic agencies, may yield better results.

¹ From the Office of Cancer Investigations, U. S. Public Health Service, Gibbs Memorial Laboratory, Harvard University, Cambridge, Mass. Read, in part, at the annual meeting of the American Association for Cancer Research, Richmond, Va., April 5, 1939.

The chemical structure of colchicine is thought to be (5):



Chemists state, with certainty, that colchicine contains a phenanthrene nucleus.

Synthesis of compounds closely related to colchicine requires laborious and prolonged investigations which are not feasible at present.

The investigations reported here were undertaken as an empirical trial of compounds whose only apparent relationship to colchicine is a phenanthrene nucleus with various substituents at different positions. No high hopes were entertained as to favorable results and no outstanding findings were made. In a few instances results were obtained which probably merit further investigation.

MATERIALS AND METHODS

Most of the tests were made in male and female strain ABC mice, about 2 months old, bearing 6- or 7-day-old transplanted sarcoma 37. In order to make the tumors more readily visible, the abdomens of the mice were shaved and the tumor mash implanted into the skin (6). In 6 days practically 100 percent of the tumors were of a uniform size, oval in shape, half an inch long by a quarter of an inch wide, and most of them without surface discolorations. A few tests were made in C₃H female mice about 9 months of age bearing spontaneous mammary tumors.

The substances tested were prepared by Small and coworkers in a search for a remedy that is pain-relieving but not habit-forming. Since we were aware that the structural formulas of those compounds somewhat resembled that of colchicine, a request was made for samples for empirical trial. Dr. Small and Dr. Mosettig were kind enough to supply small amounts of 168 such compounds, 75 of which have been tested and are reported here.

Most of the compounds were insoluble in water, but were soluble in alcohol, ethylene glycol, or other menstruum. As both alcohol and ethylene glycol are toxic to mice, most of the tests were made with distilled water. If a compound did not go into solution, dilutions were made of a suspension. The injections were made intraperitoneally in one-half cc. total volume, unless otherwise stated. Although these

substances were insoluble in distilled water, pharmacological action was attained through peritoneal absorption. The effects on tumors of insoluble bases were often as marked as those of their soluble salts. Also, by injecting the materials as suspended crystals, it was hoped that absorption would be slower and the effects prolonged.

After injection, the mice were observed for their immediate pharmacological reaction; they were examined again in 24 hours, to note effects, if any, on the tumors, while the final results were recorded in 3 weeks, at which time the transplanted tumors, if unaffected, begin to kill the mice. The results were tabulated in three categories as to whether the tumors were (a) growing, (b) smaller, or (c) gone. Where the term "regressed" is used, it is meant that no visible or palpable evidence of tumor remained. The spontaneous regression rate of transplanted S-37 dermal tumors in 200 strain ABC mice was found to be 12 percent.

EXPERIMENT 1. PHENANTHRENE DERIVATIVES SUSPENDED OR DISSOLVED IN DISTILLED WATER

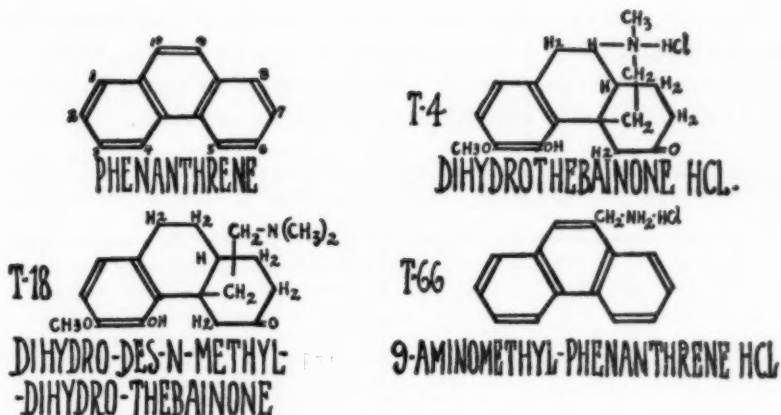
Tests were first made of the substances dissolved or suspended in distilled water. Four dilutions containing from 5 mg. to 0.005 mg. per mouse were used for each test; usually 12 mice were used to test each compound. The results were the average of all 4 dosages. Most of the substances were new; 46 of the 75 had never been tested pharmacologically.

None of the mice developed hemorrhages in tumors as a result of the treatments.

More regressions of tumors followed the use of certain groups of chemicals than of others. In 44 percent of instances the regression rate was less than the spontaneous rate of regressions. In other instances the regression rate was three or four times as great as the spontaneous regression rate. These latter rates were usually confirmed by repeated tests. The regression rate following colchicine itself, in two control experiments, was 14 percent in one test and 6 percent in the other. As with the phenanthrene compounds, doses above and below the most effective dosages were employed and the results averaged in the totals.

TABLE 1.—Experiment 1. Strain ABC mice bearing dermally transplanted S-37 tumors injected intraperitoneally (one dose) with phenanthrene derivatives suspended or dissolved in distilled water

Symbol	Name of chemical compound	Number of mice in test	Percent regressions of tumors in 3 weeks
T-1	Thebaine	15	6
T-2	Thebaine hydrochloride	24	6
T-3	Dihydrothebaine (base)	12	33
T-4	Dihydrothebaine hydrochloride	12	50
T-5	Dihydrothebaine methyl enolate:		
	Subcutaneously	23	13
	Intraperitoneally	18	0
T-6	Metathebaine	21	4
T-7	Desoxymorphine-A-salicylate	16	7
T-8	Desoxymorphine-C-hydrochloride	25	20
T-9	Dihydromorphine hydrochloride	25	5
T-10	Bromocodide hydrochloride	25	8
T-11	Dihydrodesoxycodeine-D-acid tartrate	26	15
T-12	Benzyl morphine alcoholic methyl ether hydrochloride	52	0
T-13	Dihydromorphine alcoholic ethyl ether	23	6
T-14	Alpha-iso-morphine alcoholic methyl ether (base)	19	20
T-15	Gamma-iso-morphine alcoholic methyl ether hydrochloride	19	30
T-16	Ethyl-gamma-iso-morphine hydrochloride	28	28
T-17	Des-N-methyldihydrothebaine	34	35
T-18	Dihydro-des-N-methyldihydro-thebaine	37	47
T-19	Des-N-methyldihydrothebaine methyl ether	26	19
T-20	Dihydro-des-N-methyldihydrothebaine methyl ether	11	18
T-21	Des-N-methyldihydrothebaine hydrochloride	12	0
T-22	Dihydro-des-N-methyldihydrothebaine hydrochloride	12	0
T-23	Des-N-acetyldihydro pseudo codeine enol acetate	12	0
T-24	Dihydro-des-N-methyldihydrohydroxy codeine-B	12	8
T-25	Thebenine hydrochloride	12	8
T-26	Ethebenine hydrochloride	12	16
T-27	Triacetyl-thebenine	12	8
T-28	Thebenol	12	16
T-29	Thebenone	13	0
T-30	Dihydro-des-N-methyltetrahydrodesoxycodeine hydrochloride	13	8
T-31	Des-N-methyltetrahydrodesoxycodeine	13	15
T-32	Methyl dihydro thebaine hydrochloride	13	0
T-33	Iso-methyl-di-hydrothebaine	13	0
T-34	Ethyldihydro thebaine hydrochloride	12	0
T-35	Methyldihydrocodeine enol acetate	12	8
T-36	Dihydrocodeine enol acetate	12	8
T-37	Acetylmethyldihydrothebaine hydrochloride	12	8
T-38	Isomethyl-7-ketodihydrothebaine	12	0
T-39	2 [3-diethylamino-1-oxo-propyl] 9 methyl carbazole hydrochloride	12	8
T-40	2 [3-diethylamino-1-oxo-propyl] 9-methyl carbazole hydrochloride	12	0
T-41	2 [3-diethylamino-1-oxo-propyl] 9-methyl carbazole	12	0
T-42	2 [3-dimethylamino-1-oxo-propyl] 9 methyl carbazole hydrochloride	12	16
T-43	2 [3-tetrahydroisquinolino-1-hydroxy-n-propyl] 9 methyl carbazole	13	0
T-44	3 [2-(ethylamino)-1-oxo-propyl] phenanthrene hydrochloride	13	20
T-45	3 [2-(dimethylamino)-1-oxo-propyl] phenanthrene hydrochloride	13	0
T-46	3 (2-piperidino-1-oxo-propyl) phenanthrene hydrochloride	13	0
T-47	9 (2-amino-1-oxo-propyl) phenanthrene hydrochloride	12	0
T-48	9 [2-(methylamino)-1-oxo-propyl] phenanthrene hydrochloride	13	20
T-49	9 [2-(dimethylamino)-1-oxo-propyl] phenanthrene hydrochloride	13	10
T-50	Ethylphenanthrene	13	15
T-51	2-(1-hydroxyethyl) phenanthrene	12	0
T-52	9-(1-hydroxyethyl) phenanthrene	12	16
T-53	Phenanthrene-9-carboxylic acid	12	28
T-54	3-(1 hydroxy-ethyl) phenanthrene	12	25
T-55	3 [2-(diethylamino)-1-oxo-ethyl] phenanthrene hydrochloride	12	33
T-56	3 [2-(diethylamino)-1-hydroxy-ethyl] phenanthrene	12	25
T-57	3 (2-piperidino-1-oxo-ethyl) phenanthrene hydrochloride	12	33
T-58	9 [2-(diethylamino)-1-oxo-ethyl] phenanthrene hydrochloride	12	25
T-59	9 [2-(dimethylamino)-1-hydroxy ethyl phenanthrene hydrochloride	12	16
T-60	9 (2-piperidino-1-oxo-ethyl) phenanthrene hydrochloride	11	0
T-61	Beta (9-phenanthryl) acrylic acid methyl ester	11	0
T-62	Beta (9-phenanthryl) propionic acid methyl ester	11	0
T-63	Beta (2-phenanthryl) acrylic acid	10	0
T-64	Phenanthrene-9-carboxylic acid diethylamide	12	8
T-65	Phenanthrene-3-carboxylic acid dimethylamide	14	0
T-66	9-aminomethyl phenanthrene hydrochloride	12	44
T-67	3 [2-(1, 2, 3, 4 tetrahydroisquinolino) 1-oxo-ethyl] phenanthrene hydrochloride	17	11
T-68	2 [2-(dimethylamino)-1-hydroxyethyl] phenanthrene	12	0
T-69	2 [2-(diethylamino)-1-hydroxyethyl] phenanthrene	13	0
T-70	2 (-2-piperidino-1-oxo-ethyl) phenanthrene hydrochloride	13	0
T-71	2 (-2-piperidino-1-hydroxyethyl) phenanthrene hydrochloride	12	6
T-72	2 [3-(dimethylamino)-1-oxo-propyl] phenanthrene hydrochloride	12	0
T-73	2 [3-(dimethylamino)-1-oxo-propyl] phenanthrene	14	13
T-74	2 [3-(diethylamino)-1-oxo-propyl] phenanthrene hydrochloride	15	20
T-75	2 (3-piperidino-1-oxo-propyl) phenanthrene hydrochloride	15	0



Graphic chemical formulas of phenanthrene and three phenanthrene derivatives which caused regressions of dermally transplanted sarcomas in mice.

EXPERIMENT 2. PHENANTHRENE DERIVATIVES DISSOLVED IN RECOMMENDED SOLVENTS, INJECTED SUBCUTANEOUSLY

The dissolved materials, T-1 to T-43, inclusive, were injected subcutaneously at a distance from the tumors in ABC mice bearing 6-day-old transplanted S-37 dermal tumors. Ten or more mice were used for each compound. The dosages, in most instances, were small, for increased solubility was accompanied by increased toxicity. In some instances solvents, such as ethylene glycol, were, in themselves, toxic. The solvents used were olive oil, hot distilled water, dilute hydrochloric acid (N/10), and ethylene glycol. No hemorrhages occurred in the tumors and regressions occurred in only 7 instances, as follows:

- T-17 dissolved in dilute HCl gave 10 percent tumor regression.
- T-24 dissolved in dilute HCl gave 10 percent tumor regression.
- T-26 dissolved in hot distilled water gave 10 percent tumor regression.
- T-30 dissolved in hot distilled water gave 8 percent tumor regression.
- T-32 dissolved in hot distilled water gave 10 percent tumor regression.
- T-38 dissolved in dilute HCl gave 20 percent tumor regression.
- T-42 dissolved in hot distilled water gave 33 percent tumor regression.

With 14 compounds, the tumors at the end of 3 weeks were smaller than when the injections were made. In those instances the percentage of smaller tumors ranged from 10 to 40 percent.

EXPERIMENT 3. PHENANTHRENE DERIVATIVES TESTED IN COMBINATIONS WITH COLCHICINE AND BACTERIAL FILTRATES

ABC mice bearing 6-day-old transplanted dermal S-37 tumors were injected with mixtures of the chemicals and (a) colchicine, 1 mg. per cc.; (b) *B. prodigiosus* filtrate diluted 1 to 50 (the organisms had been grown in synthetic culture medium); and (c) a 1 to 100 dilution

of a *B. prodigiosus* filtrate, the organisms of which had been cultured in broth. The doses of the chemicals, in distilled water, varied with the toxicity of the compound. An attempt was made to keep the doses of all substances below the usually effective dose.

TABLE 2.—Experiment 3. Phenanthrene derivatives mixed with (a) colchicine, and (b) bacterial filtrates and tested in ABC mice bearing transplanted dermal S-37 tumors

Phenanthrene derivatives tested	Phenanthrene derivative mixed with—			Number of mice used in tests
	Colchicine	<i>B. prodigiosus</i> filtrate organisms grown in synthetic medium	<i>B. prodigiosus</i> filtrate organisms grown in broth	
		Percent of regressions of tumors in 3 weeks		
T-1.....	40	0	6	45
T-2.....	0	0	25	40
T-3.....	15	46	30	39
T-4.....	16	15	30	38
T-5.....	20	13	21	44
T-6.....	0	20	0	30
T-7.....	22	0	0	27
T-8.....	0	0	0	27
T-9.....	0	0	0	40
T-10.....	11	11	0	27
T-11.....	0	0	0	27
T-12.....	0	0	10	28
T-13.....	44	22	0	29

A given phenanthrene compound was mixed (1) in high concentration of colchicine and low concentration of the compound, (2) in low concentration of colchicine and high concentration of the compound, and (3) medium concentrations of both. Similar mixtures were made with each of the filtrates. These mixtures were injected intraperitoneally and 27 or more mice were tested with each phenanthrene derivative. The phenanthrene derivatives in this experiment which were associated with tumor regressions were, generally speaking, the same chemicals which had been similarly effective in experiment 1.

EXPERIMENT 4. COMBINATIONS OF COMPOUNDS

Mixtures of the compounds were made in an attempt to increase the tumor regression rate. For example, 50 percent regressions of tumors had followed the use of T-4 in experiment 1; 30 percent of regressions had followed the use of T-5.

The tests were made in ABC mice bearing 6-day-old transplanted S-37 tumors. Equal parts of a solution or suspension of 0.1 gm. of each chemical in 10 cc. of distilled water were injected intraperitoneally in varying doses from 0.5 cc. to 0.025 cc.

The mixtures, as tested, did not enhance the activity of the individual compounds.

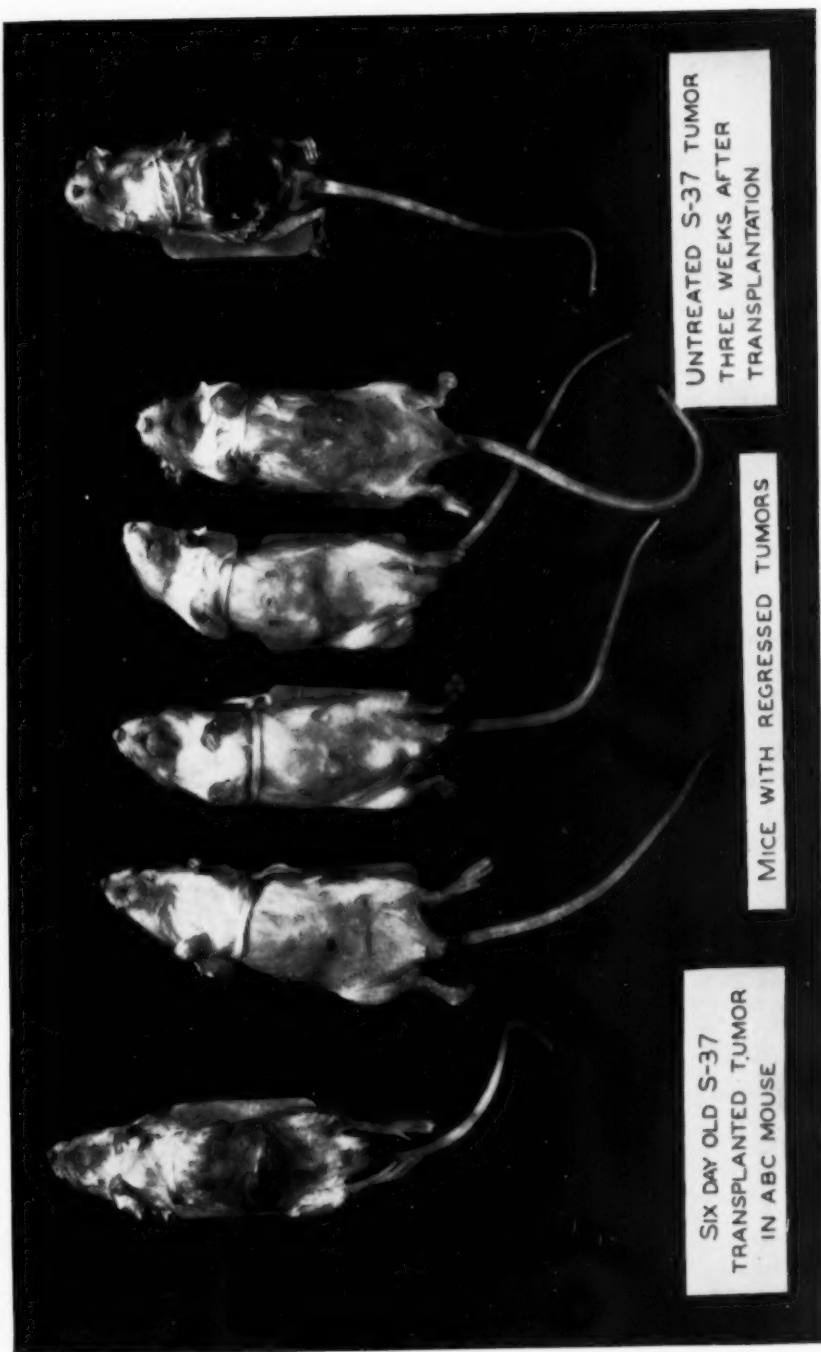


FIGURE 1.—Regressions of sarcoma 37 in strain ABC mice following treatment by phenanthrene derivatives.



TABLE 3.—*Experiment 4. Combinations of phenanthrene derivatives tested in ABC mice bearing transplanted S-37 tumors*

Mixtures of compounds	Number of mice tested	Condition of the tumors in 3 weeks		
		Percent regressions of tumors (mice living)	Mice living or dead	
			Percent of tumors smaller	Percent of tumors growing
T-4 } T-15 } mixed..... T-23 }	14	0	0	100
T-4 } T-15 } mixed..... T-25 }	14	7	7	86
T-4 } T-15 } mixed..... T-35 }	14	9	18	73

EXPERIMENT 5. MIXTURES OF LIKELY PHENANTHRENE COMPOUNDS WITH (A) THEELIN IN OIL AND (B) CHOLESTEROL

Both estrin and cholesterol contain a phenanthrene nucleus; both are biologically formed substances. Tested separately in mice, they caused no regressions in dermal sarcomas. They were mixed with several phenanthrene derivatives which had caused tumor regression in previous tests. The phenanthrene derivatives were suspended or dissolved, 100 mg. per 10 cc., in distilled water, the estrin was dissolved in peanut oil, and the cholesterol, 50 mg., was added to 3 cc. of olive oil. Equal parts were mixed and shaken in a mechanical shaker for 20 minutes prior to injection. The injections, 0.5 cc. of the mixtures, were made intraperitoneally into ABC mice bearing 6-day-old transplanted dermal tumors.

TABLE 4.—*Experiment 5. Combinations of phenanthrene derivatives with estrin and cholesterol tested in ABC mice bearing S-37 tumors*

Mixture injected	Number of mice tested	Condition of tumors in 3 weeks		
		Percent of tumors regressed (mice living)	Mice living or dead	
			Percent of tumors smaller	Percent of tumors growing
T-4, T-15, T-23, and estrin.....	15	0	0	100
T-4 and estrin.....	15	0	0	100
T-8 and estrin.....	15	6	13	81
T-15 and estrin.....	15	33	0	67
T-23 and estrin.....	14	21	21	58
T-4, T-15, and estrin.....	14	7	0	93
T-4, T-15, T-23, estrin and cholesterol.....	15	0	6	94
T-4 and cholesterol.....	14	0	0	100
T-35 and cholesterol.....	16	18	150	32
T-18, estrin, and cholesterol.....	17	5	15	80
T-4, T-15, T-23, estrin, and cholesterol.....	17	5	0	95

¹ 30 percent in this group died in 17 days.

Certain compounds, such as T-4, were less effective in these combinations than they were when tested singly, while T-35 appeared to

have an increased deleterious effect on this type of tumor. This test was made in order to determine what effects biologically formed substances would have on the actions of the phenanthrene derivatives.

EXPERIMENT 6. PHENANTHRENE DERIVATIVES TESTED (ONE DOSE) IN FEMALE C_3H MICE BEARING SPONTANEOUS MAMMARY TUMORS

The mice used in this experiment were C_3H female mice, 9 months old, raised in this laboratory by Dr. Andervont. Each mouse bore one or more spontaneous mammary tumors. The chemicals tested were T-3, T-4, T-15, T-16, T-17, T-18, T-21, T-22, T-24, T-37, and T-43. One-tenth of a gram of the chemical was dissolved or suspended in 10 cc. of distilled water. One-half a cc. of the resulting solution or suspension was injected (one dose) subcutaneously, at a distance from the tumor. Eleven phenanthrene compounds were tested in 46 mice bearing spontaneous mammary tumors. No regressions of tumors resulted.

EXPERIMENT 7. PHENANTHRENE DERIVATIVES TESTED (DAILY DOSES) IN FEMALE C_3H MICE BEARING SPONTANEOUS MAMMARY TUMORS

The mice and the materials were of the same kind as those used in experiment 6. In this test, however, daily doses of the chemicals were administered, 0.1 cc. of a solution or suspension containing 100 mg. in 10 cc. of distilled water. The injections were made subcutaneously at a distance from the tumors. The daily injections were continued for 13 days. T-4, T-8, T-17, and T-18 were tested in a total of 16 C_3H mice bearing spontaneous mammary tumors. None of the tumors regressed as a result of treatment.

TABLE 5.—Comparison of activity of 10 phenanthrene derivatives in 4 tests

Test material	Percent of regressions of 6-day-old transplanted dermal sarcomas in ABC mice in 3 weeks				Total mice used in 4 tests (573)
	Phenanthrene compounds mixed with—				
	Dis-tilled water	Colchicine	<i>B. prodigiosus</i> organisms grown in synthetic culture medium	Berkefeld filtrates organisms grown in broth	
T-1.....	5	0	0	6	60
T-2.....	5	0	0	25	64
T-3.....	33	15	46	30	51
T-4.....	50	16	15	30	50
T-5.....	13	20	13	21	85
T-6.....	4	0	20	0	51
T-7.....	7	22	0	0	43
T-8.....	20	10	10	10	52
T-9.....	5	0	0	0	65
T-10.....	8	11	11	0	52

¹ 22 percent smaller.

² 33 percent smaller.

³ 40 percent smaller.

A higher rate of regressions of transplanted tumors followed the use of certain phenanthrene derivatives than of others.

Although there is some evidence that substituents such as the carbonyl and amine groups in the 3- or the 9-position of the phenanthrene nucleus may be more active than others, no definite conclusions have yet been reached.

In a general way these results parallel the work of others in that transplanted tumors are more readily affected by chemical compounds than are spontaneous cancers (7).

SUMMARY

Seventy-five phenanthrene derivatives, the graphic chemical formulas of which resemble that of colchicine insofar as most of them contained a phenanthrene nucleus, were tested empirically in 1,841 mice bearing transplanted sarcomas and 62 mice bearing spontaneous carcinomas. Most of the compounds were new; 46 of them had never been tested pharmacologically. In mice bearing transplanted tumors, the tumor regression rate ranged from none to 50 percent. No regressions occurred in the mice bearing spontaneous tumors. No findings were made that can, as yet, be applied to the treatment of cancer in human beings.

Activity has not, as yet, been satisfactorily associated with any specific chemical grouping.

Some evidence is presented that a given chemotherapeutic agent may affect spontaneous carcinomas and transplanted sarcomas differently.

ACKNOWLEDGMENTS

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REFERENCES

- (1) Voegtlin, Carl: Biochemistry of malignant tissues. *Physiological Rev.*, **17**: 92 (1937).
- (2) Dustin, A. P.: Contribution à l'étude de l'action des poisons caryoclasiques sur les tumeurs animales. *Bull. Acad. roy. de Med. Belgique*, **14**: 487 (1934).
- Dustin, A. P.: Colchicine et cancer. *Gaz. d. hop.*, **111**: 661 (1938).
- Dermen, H.: A cytological analysis of polypoidy. *J. of Heredity*, **29**: 211 (1938).
- (3) Brues, Austin M., and Jackson, Elizabeth B.: Nuclear abnormalities resulting from inhibition of mitosis by colchicine and other substances. *Am. J. Cancer*, **30**: 504 (1937).
- Litter, J., Marble, Beula B., and Salter, Wm. T.: Relation between nuclear division and ammonia metabolism of growing tissues. *Am. J. Cancer*, **31**: 274 (1937).
- (4) Lits, F. J., Kirschbaum, A., and Strong, L.C.: Action of colchicine on transplanted malignant lymphoid neoplasm in mice of the C₃H strain. *Am. J. Cancer*, **34**: 196 (1938).
- Liebow, A. A., and Tennant, Robt.: Action of colchicine on tissue culture of breast cancer cells. *Am. J. Path.* **14**: 676 (1938).

- (5) Windaus, A.: Untersuchungen Über die Konstitution des Colchicins. *Annalen der Chemie*, **439**: 59 (1934).
Bursian, K.: Über das Colchicin. *Ber. Deutsch. Chem. Gesellsch.*, **71**: 245 (1938).
Grewe, R.: Über die Jod-methoxy-phthalsäure aus Colchicin. *Ber. Deutsch. Chem. Gesellsch.*, **71**: 907 (1938).
- (6) Andervont, H. B.: Reaction of mice and of various mouse tumors to injection of bacterial products. *Am. J. Cancer*, **27**: 77 (1936).
- (7) Haddow, A., and Robinson, A. M.: Influence of various polycyclic hydrocarbons on growth rate of transplantable tumors. *Proc. Roy. Soc., ser. B.*, **122**: 442 (1937).
Haddow, A., Scott, C. M., and Scott, J. D.: Influence of certain carcinogenic and other hydrocarbons on body growth in rat. *Proc. Roy. Soc., ser. B.*, **122**: 477 (1937).
Olitsky, P. K., and Harford, Carl: Intranuclear inclusion bodies in tissue reactions produced by injections of certain foreign substances. *Am. J. Path.*, **13**: 729 (1937).
Voegtlin, Carl: Some chemical aspects of the cancer problem. (Herter lectures) *Science*, **88**: 41 (1938).
Cook, J. W., and Kennaway, E. L.: Chemical compounds as carcinogenic agents; first supplementary report; literature of 1937. *Am. J. Cancer*, **33**: 80 (1938).
Mendel, Bruno: Action of ferricyanide on tumor cells. *Am. J. Cancer*, **30**: 549 (1937).

NEW LOW MORTALITY RATES FOR 1938

According to the latest provisional figures issued by the Bureau of the Census,¹ both the general mortality rate and the infant mortality rate for the United States reached new low levels in 1938. The provisional crude death rate for that year was 10.6 per 1,000 population and the infant mortality rate is given as 50.9 per 1,000 live births. Both of these rates are the lowest ever recorded in the respective registration areas of continental United States and no doubt represent the lowest for the country as a whole. For several earlier years these registration areas were not coextensive with the United States. The death registration area was established in 1900 and the birth registration area in 1915, and neither area included all States until 1933. The District of Columbia is included in both areas.

The nearest approach to the general mortality rate for 1938 was the rate of 10.7, in 1933, and the next lowest recorded infant mortality rate was 54.4, in 1937. The latter rate has been decreasing steadily, almost continuously, for two decades. In 1915, the year in which the birth registration area was established, the rate was 99.9 for that area, that is, one out of ten babies born died before reaching one year of age. In 1938 this rate had been cut in half, and in that year only one in twenty babies died before reaching the first birth anniversary.

The highest general mortality rate for any State in 1938 was 14.5 per 1,000, and the lowest 7.4. These rates may be compared with the rate of 17.6 for the death registration area in 1900. The highest infant mortality rate for a State in 1938 was 108.8, and the lowest 36.1. While various factors are involved in determining these rates,

¹ Vital Statistics—Special Reports, Vol. 7, Nos. 47 and 48, pp. 451-463.

such as population characteristics, climate, migration, and others, some of which are not amenable to control by health authorities, the infant mortality is considered one of the excellent criteria for evaluating health work. The maximum and minimum infant death rates for the United States for 1938, and the low rates for certain other countries, Australia, for example, where the rate has been around 40 or lower for several years, emphasize the fact that the saving of infant lives has not yet reached the maximum of efficiency in public health work in this country.

While the factors involved in achieving a new minimum death rate cannot be evaluated without a more detailed analysis of specific rates, there can be little doubt that the expansion of the public health program, improved State and local health services, and intensive public health efforts directed against specific diseases have contributed a large share. For this reason alone there should be no retrenchment in public health activities, but, rather, increased effort; not only should the high level of public health so far achieved be maintained, but it should be further improved wherever possible by intensified attacks on specific diseases and specific health problems, and by the extension of public health protection and provision of medical care to all. For it must be remembered that the general death rate does not present the complete health picture. Hidden in that rate are specific causes of death which increased public health effort can still materially reduce, long periods of illness and disability resulting from diseases with low death rates, such as malaria, and the untold suffering, crippling effects, and cost of institutional care incident to syphilis, the enormity and seriousness of which are buried under terminal or contributory causes of death.

DEATHS DURING WEEK ENDED JUNE 24, 1939

[From the Weekly Health Index, issued by the Bureau of the Census, Department of Commerce]

	Week ended June 24, 1939	Correspond- ing week, 1938
Data from 88 large cities of the United States:		
Total deaths.....	7,454	7,455
Average for 3 prior years.....	¹ 7,619	-----
Total deaths, first 25 weeks of year.....	221,987	214,228
Deaths under 1 year of age.....	452	455
Average for 3 prior years.....	¹ 510	-----
Deaths under 1 year of age, first 25 weeks of year.....	13,050	13,292
Data from industrial insurance companies:		
Policies in force.....	67,201,091	69,280,198
Number of death claims.....	12,204	11,718
Death claims per 1,000 policies in force, annual rate.....	9.5	8.8
Death claims per 1,000 policies, first 25 weeks of year, annual rate.....	11.2	9.7

¹ Data for 86 cities.

PREVALENCE OF DISEASE

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring

UNITED STATES

CURRENT WEEKLY STATE REPORTS

These reports are preliminary, and the figures are subject to change when later returns are received by the State health officers.

In these and the following tables, a zero (0) indicates a positive report and has the same significance as any other figure, while leaders (....) represent no report, with the implication that cases or deaths may have occurred but were not reported to the State health officer.

Cases of certain diseases reported by telegraph by State health officers for the week ended July 1, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median

Division and State	Diphtheria				Influenza				Measles			
	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases	1934-38 median	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases	1934-38 median	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases	1934-38 median
NEW ENG.												
Maine.....	6	1	0	0	6	1	-----	-----	308	51	81	81
New Hampshire.....	0	0	0	0	-----	-----	-----	-----	132	13	17	26
Vermont.....	0	0	0	1	-----	-----	-----	-----	2,118	158	56	35
Massachusetts.....	5	4	0	5	-----	-----	-----	-----	593	504	460	460
Rhode Island.....	0	0	2	1	-----	-----	-----	-----	458	60	1	20
Connecticut.....	3	1	0	3	-----	-----	5	1	700	236	26	49
MID. ATL.												
New York ¹	4	10	17	31	1	1	2	3	348	869	1,986	1,476
New Jersey ¹	6	5	4	10	-----	-----	2	3	32	27	232	366
Pennsylvania ^{1 2}	4	7	22	25	-----	-----	-----	-----	43	85	1,010	1,010
E. NO. CEN.												
Ohio ¹	17	22	23	20	5	7	-----	9	45	58	540	971
Indiana.....	13	9	6	7	18	12	-----	8	15	10	44	54
Illinois.....	16	24	20	37	1	2	7	11	18	28	182	490
Michigan ²	10	9	5	7	1	1	-----	-----	171	162	1,006	218
Wisconsin.....	2	1	2	2	12	7	20	14	550	313	1,245	1,178
W. NO. CEN.												
Minnesota.....	10	5	3	3	2	1	-----	-----	200	103	149	63
Iowa ¹	14	7	0	2	4	2	-----	-----	130	64	165	41
Missouri.....	8	6	1	15	-----	-----	-----	8	23	18	18	80
North Dakota.....	7	1	5	1	-----	-----	8	-----	66	9	39	11
South Dakota.....	0	0	1	1	-----	-----	-----	-----	173	23	0	0
Nebraska.....	0	0	1	1	-----	-----	-----	-----	42	11	35	21
Kansas.....	6	2	1	5	-----	-----	-----	1	56	20	67	67
SO. ATL.												
Delaware.....	0	0	0	0	-----	-----	-----	-----	39	2	4	9
Maryland ^{1 2}	3	1	6	5	-----	-----	-----	1	145	47	39	79
Dist. of Col. ¹	32	4	2	5	-----	-----	-----	-----	622	77	19	19
Virginia.....	9	5	3	6	26	14	-----	-----	216	115	126	126
West Virginia.....	13	5	4	7	19	7	6	11	40	15	87	87
North Carolina ^{1 4}	6	4	15	9	-----	-----	5	5	254	174	330	134
South Carolina ⁴	16	6	2	3	311	114	83	59	25	9	74	18
Georgia ⁴	15	9	4	5	184	111	-----	-----	27	16	0	0
Florida ⁴	15	5	7	2	-----	-----	-----	1	54	18	48	8
E. SO. CEN.												
Kentucky.....	5	3	3	3	16	9	9	2	3	2	71	71
Tennessee ¹	2	1	9	3	4	2	4	4	12	7	32	32
Alabama ⁴	5	3	3	8	9	5	16	10	83	47	62	49
Mississippi ²	20	8	4	5	-----	-----	-----	-----	-----	-----	-----	-----

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended July 1, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median—Continued

Division and State	Diphtheria				Influenza				Measles			
	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases	1934-38, median	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases	1934-38, median	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases	1934-38, median
W. SO. CEN.												
Arkansas.....	5	2	3	4	15	6	11	3	20	8	56	8
Louisiana ¹	10	4	5	6	10	4	7	7	44	18	11	5
Oklahoma.....	10	5	7	4	18	9	24	10	70	35	30	21
Texas ¹	9	11	16	20	27	32	113	59	105	127	49	100
MOUNTAIN												
Montana ¹	0	0	1	2	28	3	—	2	487	52	49	4
Idaho ¹	20	2	0	0	—	—	2	1	173	17	2	4
Wyoming ¹	0	0	0	0	—	—	—	—	720	33	2	2
Colorado ¹	120	25	13	10	39	8	—	—	197	41	48	49
New Mexico.....	12	1	1	1	12	1	4	1	185	15	18	23
Arizona.....	25	2	4	2	294	24	9	2	98	8	12	12
Utah ^{1,2}	0	0	0	0	10	1	—	—	338	34	180	6
PACIFIC												
Washington.....	0	0	0	0	—	—	—	—	1,665	540	15	124
Oregon ¹	10	2	4	1	50	10	10	10	298	60	40	16
California.....	21	25	16	25	11	13	11	17	645	787	472	515
Total.....	10	247	245	309	19	407	358	336	207	5,126	9,235	9,235
26 weeks.....	16	10,227	12,185	13,098	271	149,475	43,690	102,317	520	334,515	739,432	644,786

Division and State	Meningitis, meningococcus				Polio-myelitis				Scarlet fever			
	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases	1934-38, median	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases	1934-38, median	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases	1934-38, median
NEW ENG.												
Maine.....	0	0	0	0	6	1	0	0	84	14	9	11
New Hampshire.....	0	0	0	0	0	0	0	0	0	0	0	3
Vermont.....	0	0	0	0	0	0	0	0	54	4	3	4
Massachusetts.....	0	0	0	2	1.2	1	0	1	71	60	130	130
Rhode Island.....	0	0	0	0	0	0	0	0	53	7	5	10
Connecticut.....	0	0	0	0	0	0	0	0	42	14	24	24
MID. ATL.												
New York ¹	1.2	3	6	6	1.2	3	2	3	62	154	226	202
New Jersey ¹	1.2	1	0	1	0	0	0	2	69	58	29	61
Pennsylvania ^{1,2}	4	8	4	5	0	0	0	1	28	55	286	253
E. NO. CEN.												
Ohio ¹	1.5	2	1	2	0.8	1	1	1	124	161	116	152
Indiana.....	0	0	2	1	0	0	0	0	39	26	17	41
Illinois.....	0.7	1	1	7	1.3	2	4	3	61	93	154	209
Michigan ¹	0	0	0	2	2.1	2	0	1	157	149	126	196
Wisconsin.....	7	4	2	2	0	0	0	0	79	45	60	173
W. NO. CEN.												
Minnesota.....	0	0	0	1	0	0	0	0	37	19	27	49
Iowa ¹	4	2	0	1	0	0	1	0	34	17	15	31
Missouri.....	1.3	1	3	2	0	0	0	0	35	27	16	25
North Dakota.....	7	1	0	0	0	0	1	0	15	2	2	8
South Dakota.....	8	1	0	0	0	0	1	0	113	15	5	8
Nebraska.....	4	1	0	0	0	0	0	0	11	3	16	10
Kansas.....	0	0	0	0	0	0	0	1	95	34	20	23

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended July 1, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median—Continued

Division and State	Meningitis, meningo-coccus				Poliomyelitis				Scarlet fever			
	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases	1934-38, median	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases	1934-38, median	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases	1934-38, median
SO. ATL.												
Delaware.....	0	0	0	0	0	0	0	0	59	3	3	2
Maryland ^{1 2}	0	0	1	1	0	0	0	0	19	6	19	19
Dist. of Col. ¹	0	0	0	0	0	0	0	0	16	2	8	0
Virginia.....	1.9	1	5	4	0	0	2	1	6	3	4	10
West Virginia.....	0	0	1	2	0	0	0	0	32	12	13	18
North Carolina ^{1 4}	4	3	0	3	4	3	2	2	18	12	16	14
South Carolina ⁴	0	0	1	0	79	29	0	1	14	5	1	1
Georgia ⁴	0	0	0	0	7	4	3	1	18	11	8	5
Florida ⁴	0	0	0	0	0	0	1	1	6	2	0	1
E. SO. CEN.												
Kentucky.....	1.7	1	6	5	0	0	1	1	26	15	8	12
Tennessee ¹	0	0	0	2	1.8	1	1	1	21	12	6	5
Alabama ⁴	0	0	4	2	1.8	1	5	5	26	15	7	4
Mississippi ³	0	0	0	0	0	0	3	2	3	1	2	8
W. SO. CEN.												
Arkansas.....	2.5	1	0	0	2.5	1	0	0	8	2	2	2
Louisiana ⁴	0	0	1	1	0	0	3	3	12	5	6	6
Oklahoma.....	0	0	1	0	2	1	0	0	18	9	7	7
Texas ⁴	0.8	1	0	0	7	9	1	2	15	18	42	32
MOUNTAIN												
Montana ¹	0	0	0	0	9	1	0	0	19	2	4	9
Idaho ¹	0	0	0	0	0	0	0	0	20	2	0	2
Wyoming ¹	0	0	0	0	0	0	0	0	131	6	7	7
Colorado ⁸	0	0	0	0	5	1	0	0	217	45	17	13
New Mexico.....	12	1	0	0	12	1	0	0	124	10	6	6
Arizona.....	0	0	1	1	12	1	0	0	110	9	3	7
Utah ^{1 2}	0	0	0	0	10	1	0	0	40	4	17	11
PACIFIC												
Washington.....	0	0	0	1	0	0	0	1	19	6	11	19
Oregon.....	0	0	0	0	0	0	0	0	30	6	20	20
California.....	0.8	1	1	5	13	16	1	7	80	97	97	113
Total.....	1.4	34	41	61	3	80	33	158	51	1,277	1,617	2,228
26 weeks.....	1.8	1,173	1,898	3,630	1.2	793	547	815	170	110,798	130,360	157,273

Division and State	Smallpox				Typhoid and paratyphoid fever				Whooping cough		
	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases	1934-38, median	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases	1934-38, median	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases
NEW ENG.											
Maine.....	0	0	0	0	18	3	0	1	229	38	46
New Hampshire.....	0	0	0	0	0	0	1	0	0	0	0
Vermont.....	0	0	0	0	0	0	1	0	590	44	26
Massachusetts.....	0	0	0	0	2	2	0	0	120	102	79
Rhode Island.....	0	0	0	0	0	0	0	0	137	18	13
Connecticut.....	18	6	0	0	6	2	2	1	217	73	101
MID. ATL.											
New York ¹	0	0	0	0	4	11	8	11	159	396	472
New Jersey ¹	0	0	0	0	5	4	4	3	356	299	161
Pennsylvania ^{1 2}	0	0	0	0	3	5	25	17	160	316	332

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended July 1, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median—Continued

Division and State	Smallpox				Typhoid and paratyphoid fever				Whooping cough		
	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases	1934-38, median	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases	1934-38, median	July 1, 1939, rate	July 1, 1939, cases	July 2, 1938, cases
E. NO. CEN.											
Ohio ¹	5	7	1	0	5	6	8	8	257	334	213
Indiana.....	10	7	19	3	4	3	2	5	119	80	13
Illinois.....	9	14	21	21	6	9	16	16	198	302	245
Michigan ²	2	2	0	0	3	3	3	4	220	208	287
Wisconsin.....	2	1	2	6	4	2	0	0	301	171	207
W. NO. CEN.											
Minnesota.....	6	3	23	7	6	3	0	0	68	35	25
Iowa ¹	24	12	12	12	12	6	0	1	101	50	19
Missouri.....	17	13	17	10	17	13	3	18	80	62	30
North Dakota.....	0	0	3	3	0	0	0	0	51	7	19
South Dakota.....	53	7	4	4	0	0	0	0	30	4	6
Nebraska.....	4	1	0	2	0	0	0	0	19	5	9
Kansas.....	0	0	7	7	14	5	0	6	39	14	110
SO. ATL.											
Delaware.....	0	0	0	0	39	2	3	1	59	3	11
Maryland ¹	0	0	0	0	3	1	3	4	176	57	56
Dist. of Col. ¹	0	0	0	0	0	0	0	0	234	29	5
Virginia.....	0	0	0	0	22	12	7	8	75	40	54
West Virginia.....	0	0	0	0	30	11	6	6	56	21	77
North Carolina ¹	0	0	0	0	12	8	20	20	370	253	356
South Carolina ¹	3	1	0	0	44	16	22	20	120	44	84
Georgia ¹	0	0	0	0	50	30	25	34	46	28	44
Florida ¹	0	0	0	0	6	2	2	4	21	7	17
E. SO. CEN.											
Kentucky.....	0	0	0	0	21	12	18	18	19	11	46
Tennessee ¹	4	2	1	1	26	15	11	27	183	104	45
Alabama ¹	0	0	0	0	12	7	14	17	97	55	51
Mississippi ²	0	0	3	0	18	7	15	16			
W. SO. CEN.											
Arkansas.....	7	3	1	0	32	13	17	17	35	14	37
Louisiana ¹	0	0	0	0	53	22	21	21	15	6	43
Oklahoma.....	12	6	8	1	48	24	10	9	8	4	25
Texas ¹	4	5	13	2	17	21	53	35	161	194	258
MOUNTAIN											
Montana ¹	9	1	1	2	0	0	1	1	84	9	52
Idaho ¹	0	0	13	3	51	5	3	2	61	6	5
Wyoming ¹	44	2	0	1	0	0	0	0	44	2	16
Colorado ¹	0	0	0	0	0	0	2	2	149	31	32
New Mexico.....	0	0	4	1	86	7	9	7	222	18	15
Arizona.....	25	2	2	0	25	2	9	4	319	26	0
Utah ¹	60	6	0	0	20	2	1	0	685	69	96
PACIFIC											
Washington.....	0	0	3	3	3	1	3	3	22	7	66
Oregon ¹	0	0	7	5	0	0	4	4	134	27	26
California.....	6	7	22	2	7	8	10	10	103	126	206
Total	4	108	187	152	12	305	359	421	152	3,749	4,136
26 weeks	13	8,272	11,937	5,573	6	3,803	4,298	4,298	158	101,777	111,737

¹ Rocky Mountain spotted fever, week ended July 1, 1939, 35 cases as follows: New York, 3; New Jersey, 3; Pennsylvania, 3; Ohio, 2; Iowa, 3; Maryland, 4; District of Columbia, 2; North Carolina, 4; Tennessee, 1; Montana, 1; Idaho, 2; Wyoming, 2; Utah, 3; Oregon, 2.

² New York City only.

³ Period ended earlier than Saturday.

⁴ Typhus fever, week ended July 1, 1939, 44 cases as follows: North Carolina, 2; South Carolina, 1; Georgia, 17; Florida, 3; Alabama, 13; Louisiana, 2; Texas, 6.

⁵ Colorado tick fever, week ended July 1, 1939, Colorado, 4 cases.

SUMMARY OF MONTHLY REPORTS FROM STATES

The following summary of cases reported monthly by States is published weekly and covers only those States from which reports are received during the current week.

State	Men- gitis, menin- gococ- cus	Diph- theria	Infl- enza	Ma- laria	Mea- sles	Pel- lagra	Pollo- mye- litis	Scarlet fever	Small- pox	Ty- phoid and paraty- phoid fever
<i>May 1939</i>										
Arizona.....	0	7	198	8	138	4	10	55	23	7
Hawaii Territory.....	0	8	23		16		2	2	0	2
New York.....	20	69		2	9,782		3	2,321	16	28
North Carolina.....	4	37	30	71	2,708	24	2	71	0	26
Oregon.....		3	145		312			62	45	11
Virginia.....	0	32	398	11	3,187	17	0	64	0	11

<i>May 1939</i>		<i>May 1939</i>		<i>May 1939</i>	
	Cases		Cases		Cases
Chickenpox:		Impetigo contagiosa:		Trachoma:	
Arizona.....	62	Hawaii Territory.....	21	Arizona.....	60
Hawaii Territory.....	156	Oregon.....	24	Hawaii Territory.....	1
New York.....	2,505	Leprosy:		Trichinosis:	
North Carolina.....	435	Hawaii Territory.....	4	New York.....	1
Oregon.....	138	Mumps:		Tularaemia:	
Virginia.....	414	Arizona.....	55	Arizona.....	2
Conjunctivitis, infectious:		Hawaii Territory.....	256	New York.....	1
Hawaii Territory.....	36	Oregon.....	100	North Carolina.....	1
Dysentery:		Virginia.....	295	Virginia.....	4
Arizona.....	179	Ophthalmia neonatorum:		Typhus fever:	
Hawaii Territory (am- oebic).....	1	New York.....	19	Hawaii Territory.....	1
Hawaii Territory (bacil- lary).....	1	Rabies in animals:		New York.....	2
New York (amoebic).....	35	New York ¹	7	North Carolina.....	4
Virginia (amoebic).....	1	Oregon.....	1	Undulant fever:	
Virginia (bacillary).....	245	Rocky Mountain spotted fever:		Arizona.....	4
Encephalitis, epidemic or lethargic:		New York.....	1	New York.....	17
Hawaii Territory.....	1	Oregon.....	15	North Carolina.....	1
New York.....	10	Virginia.....	3	Virginia.....	2
Virginia.....	2	Scabies:		Vincent's infection:	
German measles:		Oregon.....	4	New York ¹	63
Arizona.....	4	Septic sore throat:		Oregon.....	7
New York.....	161	Hawaii Territory.....	1	Whooping cough:	
North Carolina.....	31	New York.....	246	Arizona.....	60
Hookworm disease:		North Carolina.....	8	Hawaii Territory.....	635
Hawaii Territory.....	10	Virginia.....	78	New York.....	1,835
		Tetanus:		North Carolina.....	1,056
		Hawaii Territory.....	4	Oregon.....	47
		New York.....	8	Virginia.....	220

¹ Exclusive of New York City.

PLAGUE INFECTION IN IDAHO AND OREGON

Under date of June 28, 1939, Senior Surg. C. R. Eskey reported plague infection found in Idaho and Oregon as follows:

IN FLEAS FROM GROUND SQUIRRELS IN FREMONT COUNTY, IDAHO

In a pool of 207 fleas from 167 ground squirrels, *C. armatus*, shot June 14 at a location 20 miles northwest of Macks Inn.

IN GROUND SQUIRRELS AND FLEAS FROM GROUND SQUIRRELS IN WALLOWA COUNTY, OREG.

In tissue from 2 ground squirrels, *C. columbianus*, proved separately, shot June 4, 1939, on a ranch 29 miles northeast of Enterprise, and in a pool of 20 fleas from 3 ground squirrels of the same species shot at the same time on the same ranch.

WEEKLY REPORTS FROM CITIES

City reports for week ended June 24, 1939

This table summarizes the reports received weekly from a selected list of 140 cities for the purpose of showing a cross section of the current urban incidence of the communicable diseases listed in the table.

State and city	Diph- theria cases	Influenza		Meas- les cases	Pneu- monia deaths	Scar- let fever cases	Small- pox cases	Tuber- culosis deaths	Ty- phoid fever cases	Whoop- ing cough cases	Deaths, all causes
		Cases	Deaths								
Data for 90 cities: 5-year average.....	136	40	18	3,420	384	1,086	12	379	49	1,280	-----
Current week ¹	78	33	16	1,869	250	584	5	320	28	1,260	-----
Maine:											
Portland.....	0		0	1	0	0	0	1	0	17	13
New Hampshire:											
Concord.....											
Manchester.....	0		0	0	0	0	0	0	0	0	6
Nashua.....	0		0	1	0	0	0	0	0	0	7
Vermont:											
Barre.....	0		0	0	0	0	0	0	0	1	2
Burlington.....	0		0	14	0	0	0	0	0	1	10
Rutland.....	0		0	0	0	0	0	0	0	0	5
Massachusetts:											
Boston.....	0		0	142	11	33	0	6	1	29	195
Fall River.....	0		0	0	2	0	0	0	0	2	21
Springfield.....	0		0	9	2	2	0	0	0	0	33
Worcester.....	0		0	19	7	2	0	2	0	16	49
Rhode Island:											
Pawtucket.....	0		0	8	2	1	0	0	0	0	16
Providence.....	1		0	69	1	5	0	2	1	41	64
Connecticut:											
Bridgeport.....	0		0	12	1	4	0	0	0	0	23
Hartford.....	0		0	7	2	5	0	5	0	8	35
New Haven.....	0	2	0	121	3	0	0	1	1	6	44
New York:											
Buffalo.....	1		0	50	9	18	0	7	0	17	148
New York.....	15	4	1	158	39	83	0	72	5	104	1,270
Rochester.....	0	2	0	70	0	10	0	1	2	2	50
Syracuse.....	0		0	56	3	9	0	1	0	29	44
New Jersey:											
Camden.....	1		0	0	2	0	0	1	1	8	23
Newark.....	0		0	1	2	9	0	4	0	48	89
Trenton.....	0		0	1	2	5	0	5	0	0	41
Pennsylvania:											
Philadelphia.....	1		0	59	8	22	0	14	6	140	386
Pittsburgh.....	1		1	5	7	19	0	2	0	49	138
Reading.....	1		0	6	0	0	0	0	0	0	9
Scranton.....	0			1		3	0		0	0	-----
Ohio:											
Cincinnati.....	2		0	0	1	12	0	5	0	11	114
Cleveland.....	1	2	0	2	8	19	0	8	0	65	162
Columbus.....	0		0	8	2	1	0	1	0	1	81
Toledo.....	0	1	0	19	2	3	1	1	0	37	53
Indiana:											
Anderson.....	0		0	0	0	1	1	0	0	1	4
Fort Wayne.....											
Indianapolis.....	0		1	2	3	9	0	2	0	42	83
Muncie.....	0		0	0	0	0	0	0	0	0	6
South Bend.....	0		0	1	0	1	0	0	0	10	13
Terre Haute.....	0		0	0	1	0	0	0	0	0	11
Illinois:											
Alton.....	1		0	0	0	0	0	1	0	0	12
Chicago.....	12	2	0	8	11	99	0	43	0	88	592
Elgin.....	0		0	0	0	0	0	0	0	4	9
Moline.....	0		0	0	0	1	0	0	0	1	16
Springfield.....	0		0	0	1	0	0	0	0	3	17
Michigan:											
Detroit.....	3		1	49	8	60	0	15	0	76	219
Flint.....	0		0	17	2	3	0	0	0	1	32
Grand Rapids.....	0		0	1	0	18	0	0	1	1	26
Wisconsin:											
Kenosha.....	0		0	0	0	0	0	0	0	4	3
Madison.....	0		0	68	2	0	0	0	1	16	9
Milwaukee.....	0	1	1	1	1	16	0	2	0	26	92
Racine.....	0		0	0	0	1	0	0	0	5	6
Superior.....	0		0	9	0	1	0	0	0	0	8

¹ Figures for Concord, Fort Wayne, and St. Joseph estimated; reports not received.

City reports for week ended June 24, 1939—Continued

State and city	Diph- theria cases	Influenza		Meas- les cases	Pneu- monia deaths	Scar- let fever cases	Small- pox cases	Tuber- culosis deaths	Ty- phoid fever cases	Whoop- ing cough cases	Deaths, all causes
		Cases	Deaths								
Minnesota:											
Duluth	0		0	2	0	3	0	0	0	3	20
Minneapolis	0			11	2	7	0	2	0	7	99
St. Paul	0		0	6	0	1	0	3	0	6	61
Iowa:											
Cedar Rapids	0			9		0	0		0	0	
Davenport	1			0		2	0		0	1	
Des Moines	0		0	1	0	2	0	0	0	2	37
Sioux City	0			3		2	0		0	0	
Waterloo	1			1		1	0		0	4	
Missouri:											
Kansas City	1		0	2	2	3	0	4	0	3	89
St. Joseph											
St. Louis	0		0	2	10	14	0	7	1	22	198
North Dakota:											
Fargo	0		0	1	1	1	0	0	0	0	8
Grand Forks	0			0		1	0		0	0	
South Dakota:											
Aberdeen	0			3		0	0		0	0	
Sioux Falls	0		0	0	0	2	0	0	0	0	9
Nebraska:											
Lincoln	0			2		2	0		0	19	
Omaha	0		0	5	5	0	3	2	0	3	55
Kansas:											
Lawrence	0		0	1	0	0	0	0	0	1	3
Topeka	0	2	2	2	1	2	0	0	0	0	13
Wichita	1		0	17	5	1	1	0	0	2	32
Delaware:											
Wilmington	0		0	7	1	1	0	2	0	1	21
Maryland:											
Baltimore	1		0	32	3	7	0	15	0	60	177
Cumberland	0		0	0	1	0	0	0	0	0	17
Frederick	0		0	0	0	0	0	0	0	0	2
District of Colum- bia:											
Washington	1	1	1	96	3	5	0	12	0	54	141
Virginia:											
Lynchburg	1		0	17	0	1	0	0	0	44	9
Norfolk	0		0	3	0	0	0	1	0	2	32
Richmond	1		0	80	1	2	0	0	0	2	85
Roanoke	0		0	5	1	0	0	0	0	2	19
West Virginia:											
Charleston	0		0	0	0	0	0	0	0	1	6
Huntington	1		0	0		0	0		0	0	
Wheeling	0		0	0	1	0	0	0	0	3	17
North Carolina:											
Gastonia	0			0		0	0		0	0	
Raleigh	2		0	0	1	0	0	0	0	6	18
Wilmington	0		0	0	0	0	0	0	1	2	14
Winston-Salem	0		0	1	1	0	0	1	0	0	14
South Carolina:											
Charleston	0	1	0	0	3	0	0	0	0	0	25
Florence	0		0	0	0	0	0	0	0	0	9
Greenville	0		0	0	0	0	0	0	0	0	9
Georgia:											
Atlanta	0	1	1	3	2	0	0	4	0	2	80
Brunswick	0		0	1	0	0	0	0	1	3	5
Savannah	0	2	0	3	1	1	0	2	2	11	25
Florida:											
Miami	0		0	0	3	1	0	0	1	3	20
Tampa	2		0	17	0	2	0	0	0	0	20
Kentucky:											
Ashland	0		0	0	0	0	0	2	0	0	8
Covington	0		0	0	0	0	0	2	0	0	10
Lexington	0		0	0	1	0	0	0	0	0	19
Louisville	0	1	0	2	2	4	0	3	0	17	71
Tennessee:											
Knoxville	0		0	0	0	1	0	0	0	4	20
Memphis	0		1	2	6	2	0	5	0	28	71
Nashville	0		0	1	1	1	0	3	0	8	56
Alabama:											
Birmingham	0	3	0	1	1	1	0	1	0	5	57
Mobile	0		0	0	2	1	0	0	0	0	16
Montgomery	0	1		8		0	0		0	3	
Arkansas:											
Fort Smith	0			0		2	0		0	0	
Little Rock	0		1	0	5	0	0	2	0	0	10

City reports for week ended June 24, 1939—Continued

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Small-pox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
Louisiana:											
Lake Charles.....	0	-----	0	0	1	0	0	1	0	0	12
New Orleans.....	3	1	1	9	8	3	0	5	0	33	139
Shreveport.....	0	-----	0	0	2	0	0	2	0	0	38
Oklahoma:											
Oklahoma City.....	0	-----	0	7	1	0	0	1	0	0	31
Texas:											
Dallas.....	1	-----	0	5	0	4	0	3	1	3	53
Fort Worth.....	1	-----	0	1	2	2	0	0	0	0	39
Galveston.....	0	-----	0	0	0	1	0	0	1	1	15
Houston.....	2	-----	0	3	10	0	0	6	1	1	102
San Antonio.....	1	-----	0	2	6	0	0	5	0	0	84
Montana:											
Billings.....	0	-----	0	0	2	0	0	0	0	0	6
Great Falls.....	0	-----	0	25	1	0	0	0	0	0	13
Helena.....	0	-----	0	1	0	0	0	0	0	0	3
Missoula.....	0	-----	0	0	1	0	0	1	0	0	8
Idaho:											
Boise.....	0	-----	0	1	2	0	0	0	0	0	7
Colorado:											
Colorado Springs.....	0	-----	0	0	3	8	0	2	0	0	12
Denver.....	9	-----	0	25	4	10	0	4	2	23	71
Pueblo.....	0	-----	0	3	1	1	0	0	0	8	7
New Mexico:											
Albuquerque.....	0	-----	0	0	1	2	0	1	0	0	11
Utah:											
Salt Lake City.....	0	-----	0	6	0	2	0	0	0	16	21
Washington:											
Seattle.....	0	-----	0	314	1	4	0	4	0	7	94
Spokane.....	0	-----	0	28	0	1	0	1	0	0	25
Tacoma.....	0	-----	1	9	1	2	0	0	0	0	24
Oregon:											
Portland.....	0	1	0	4	2	2	0	1	0	2	65
Salem.....	0	-----	0	0	0	0	0	0	0	0	-----
California:											
Los Angeles.....	9	9	0	209	5	22	0	14	0	31	291
Sacramento.....	1	-----	0	27	0	3	0	0	0	2	22
San Francisco.....	3	-----	0	4	5	5	0	9	0	7	189

State and city	Meningitis, meningococcus		Polio-myelitis cases	State and city	Meningitis, meningococcus		Polio-myelitis cases
	Cases	Deaths			Cases	Deaths	
Massachusetts:				South Carolina:			
Worcester.....	1	0	0	Charleston.....	0	0	6
New York:				Georgia:			
New York.....	0	0	1	Atlanta.....	0	0	1
Pennsylvania:				Florida:			
Scranton.....	1	0	0	Miami.....	0	0	1
Indiana:				Alabama:			
Indianapolis.....	0	0	1	Birmingham.....	1	0	0
Illinois:				Arkansas:			
Chicago.....	1	0	0	Little Rock.....	0	0	1
Minnesota:				Louisiana:			
Minneapolis.....	1	0	0	Shreveport.....	0	1	0
St. Paul.....	0	0	1	Texas:			
Missouri:				Dallas.....	0	0	1
St. Louis.....	1	1	0	Houston.....	1	0	0
Nebraska:				Colorado:			
Omaha.....	0	0	1	Denver.....	0	0	2
Maryland:				California:			
Baltimore.....	1	0	0	Los Angeles.....	0	0	6
Virginia:							
Richmond.....	1	0	0				

Pellagra.—Cases: Philadelphia, 1; Winston-Salem, 1; Savannah, 8; Memphis, 1.

Typhus fever.—Cases: Savannah, 1; Tampa, 1; Mobile, 2.

FOREIGN AND INSULAR

CANADA

Provinces—Communicable diseases—Week ended June 10, 1939.—During the week ended June 10, 1939, cases of certain communicable diseases were reported by the Department of Pensions and National Health of Canada as follows:

Disease	Prince Edward Island	Nova Scotia	New Brun- swick	Que- bec	Ontar- io	Mani- toba	Sas- katch- ewan	Alber- ta	British Colum- bia	Total
Cerebrospinal meningitis				2		1				3
Chickenpox		5	2	141	274	47	15	9	36	529
Diphtheria		1		53	2	4	1	1	1	63
Dysentery					2					2
Influenza		42			15		7		231	295
Lethargic encephalitis							1			1
Measles		16	1	639	1,229	6		19	24	1,934
Mumps				25	57	20		2	10	114
Pneumonia		8			12			1	5	26
Poliomyelitis						1				1
Scarlet fever		10	32	95	112	11		21		299
Tuberculosis	1	11	29	108	56	4	17	2	9	228
Typhoid and paratyphoid fever				11	3	2	1	1		18
Whooping cough		16		64	98	185	18	2	63	440

FINLAND

Communicable diseases—May 1939.—During the month of May 1939, cases of certain communicable diseases were reported in Finland as follows:

Disease	Cases	Disease	Cases
Diphtheria	176	Poliomyelitis	9
Influenza	4,220	Scarlet fever	749
Paratyphoid fever	42	Typhoid fever	6

SWITZERLAND

Communicable diseases—April 1939.—During the month of April 1939, cases of certain communicable diseases were reported in Switzerland as follows:

Disease	Cases	Disease	Cases
Cerebrospinal meningitis	8	Paratyphoid fever	6
Chickenpox	74	Poliomyelitis	1
Diphtheria and croup	33	Scarlet fever	287
German measles	15	Tuberculosis	235
Influenza	34	Typhoid fever	3
Lethargic encephalitis	1	Undulant fever	15
Measles	18	Whooping cough	77
Mumps	111		

CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER

NOTE.—A table giving current information of the world prevalence of quarantinable diseases appeared in the PUBLIC HEALTH REPORTS for June 30, 1939, pages 1182-1194. A similar cumulative table will appear in future issues of the PUBLIC HEALTH REPORTS for the last Friday of each month.

Cholera

Afghanistan—Kandahar Province—Greshk.—During the week ended July 1, 1939, 5 cases of cholera were reported in Greshk, Kandahar Province, Afghanistan.

China.—According to information dated June 28, 1939, 5 new cases of cholera were reported in Canton and vicinity between June 15 and 23, 1939. The report also states that, according to Japanese authorities, 548 cases of cholera with 272 deaths have occurred in the occupied area near Canton up to June 15, 1939. During the week ended June 24, 1939, 50 cases of cholera were reported in Hong Kong, China.

Plague

India—Rangoon.—During the week ended June 24, 1939, one case of plague was reported in Rangoon, India.

United States.—A report of plague infection in Fremont County, Idaho, and Wallowa County, Oreg., appears on page 1294 of this issue of the PUBLIC HEALTH REPORTS.

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